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Lipoproteins and Atherosclerosis

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WHETHER or not the pathogenesis of atherosclerosis involves lipids as a primary etiologic agent, a subject of considerable controversy, there can be no question but that somewhere in the pathogenesis lipids become involved as prominent components of the actual lesions. Certainly no one would contest that this process is, at least when minimal, a focal process, influenced by local factors in the arterial wall. Nonetheless such considerations may all be valid without in any way being exclusive of the possibility that blood lipids in transport may represent the source of the lipids seen in atheromata.

The authors (5, 6, 9) have presented evidence demonstrating that certain blood lipoproteins are intimately associated with atherosclerosis both in the human and in the cholesterol-fed rabbit. These studies, based upon the ultracentrifugal analysis of serum for its lipid-bearing constituents, have been carried further. It is the purpose of this discussion to report certain aspects of the progress of this particular research. The basic theory of use of the ultracentrifuge in studies of this sort is described in previous publications (4, 5, 6, 9).

Blood Lipid Transport

The true nature and significance of the state of blood lipids, such as neutral fat, fatty acids, phospholipids, cholesterol, and cholesterol esters had, in the past, been considerably obscured by the fact that most studies centered around the total analytically determinable lipid constituent, e.g., cholesterol or cholesterol ester. Actually a constituent such as cholesterol, a cholesterol ester, phospholipid, or neutral fat is present as a building block in a variety of very large molecules (up to millions of molecular weight units).

The particular significance of this fact is that from a chemical determination of a substance such as cholesterol in the blood, one is not able to predict, in any particular case, how the cholesterol is distributed among the numerous macromolecules that may exist in serum. This raises the possibility of overlooking significant molecules, with respect to disease pathogenesis, unless one is able to characterize and quantitate the various individual molecules present, no matter what the total serum level of a particular constituent building block may be, e.g., cholesterol or cholesterol ester. It is for the detection, on a quantitative basis, of these individual macromolecules bearing various lipids that the ultracentrifuge is especially useful.

Ultracentrifugal Characterization of Human Serum Lipids

The rate of movement (sedimentation or flotation) of dissolved molecules in an ultracentrifugal field depends primarily upon size, shape, and density of the molecule and the density and viscosity of the medium in which it is present. A minimum of ten distinct species of lipoproteins that may be found in human serum, differing from one another physically

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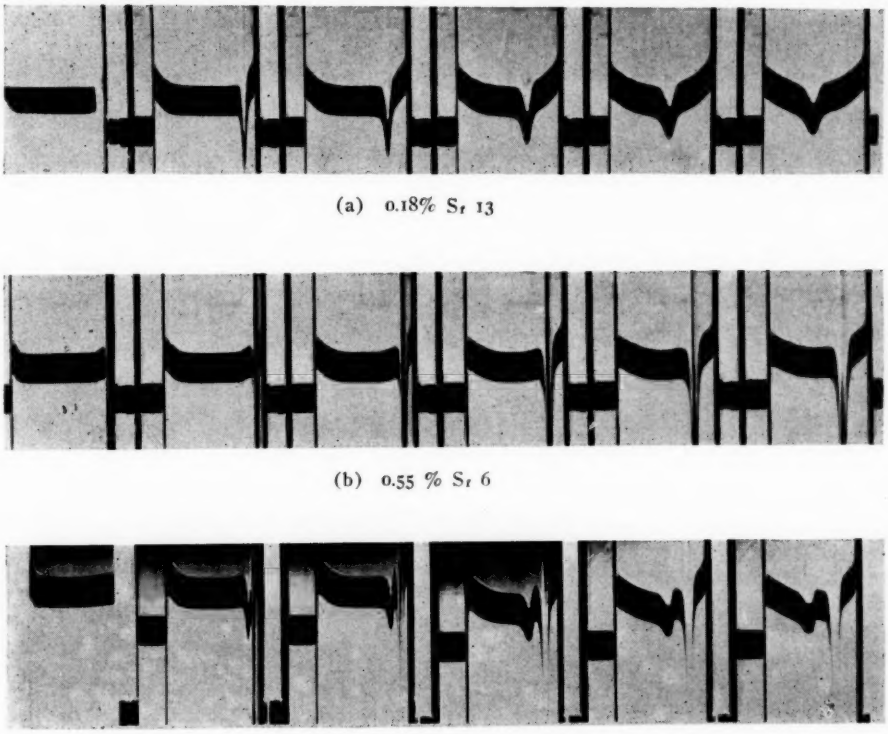
in density of the molecule and in ultracentrifugal flotation rates, have been described (9). Broadly the lipoproteins may be segregated into two major groups, the so-called low density lipoproteins (density less than 1.063) and the high density lipoproteins (density greater than 1.063). In this study of atherosclerosis attention will be confined to flotation of the low-density group of molecules.

As a preliminary operation in the study of sera for these molecules a separation is made in the preparative ultracentrifuge. In this process a density increment is given the serum sample by dilution with a concentrated sodium chloride solution. Ultracentrifugation of this serum solution for thirteen hours results in the flotation to the top of the preparative tube of all lipoprotein molecules less dense than the solution. Also during the ultracentrifugation all large molecules of density greater than the solution undergo sedimentation. Thus after a critical time of ultracentrifugation the low density group of lipoproteins will have collected as a layer at the top of the preparative tube and all the proteins and dense lipoproteins will have sedimented out of the top portion of the preparative tube.

After the centrifuge stops, removal of the top fraction containing the layered low-density lipoproteins can be effected using a capillary pipette. Next the isolated low-density lipoproteins (the top fraction) are studied in the analytic ultracentrifuge. Here the lipoprotein molecules are characterized and identified by their flotation rates. Flotation rates are given in S_f units (Svedbergs of flotation) under the specified conditions. Usually the samples are centrifuged at 52,640 RPM (forces approximately 200,000 to 250,000 x gravity) for less than one hour, with a series of photographs being taken at various stages of the flotation.

1 S_f unit = flotation rate of 1×10^{-13} cm/sec/dyne/gm. The specified conditions for these studies refer to use of a sodium chloride solution of density 1.063 gms/cc at 26°C. If runs are performed under any other conditions, appropriate corrections must be made. Spinco Model L and Model E ultracentrifuges were used throughout.

A special optical system allows the moving boundaries of macromolecules to be observed and recorded while the centrifuge is in operation. The basis for detection of these boundaries is the abrupt change in refractive index from the region of solution containing the particular class of large molecules to the region out of which these molecules have migrated. The optical system records such a refractive index change as an inverted peak for floating boundaries, the area over the peak providing a measure of the concentration of these molecules. Thus the concentration and flotation rates of the large molecules present in a solution can be determined.



(a) 0.18% S_f 13

(b) 0.55 % S_f 6

(c)

MIXTURE CONTAINING 0.13% S_f 13 & 0.55% S_f 6
FLOTATION OF ISOLATED S_f 13, S_f 6, & MIXTURE

FIG. 1

(a) Upper pattern showing flotation of isolated S_f 13 molecules.
(b) Middle pattern showing flotation of isolated S_f 6 molecules.
(c) Lower pattern showing flotation of mixture of these two lipoproteins.

Figure 1a shows the type of ultracentrifugal pattern obtained for a single molecular species of flotation rate 13 S_f units, 1b shows a single molecular species of rate 6 S_f units, and 1c shows a mixture of these two species. In practice the low-density group of lipoproteins found in human serum may comprise from one to more than one species of components, differing one from another in size, density, and chemical composition. Thus, the diagrams obtained may be considerably more complicated than the illustration of two components shown in figure 1c. In fact, the individual components may have flotation rates so close together as to be resolvable with difficulty. A typical flotation pattern illustrates the nature of the problem (fig. 2a).

Knowing the type of components (three) which exist, it is possible to resolve such a patten into its individual constituents. (fig. 2b). Figure 3 shows six illustrative ultracentrifugal patterns from humans in various clinical categories. In human serum the following classes of lipoprotein molecules have been identified:

Flotation Rate	*Density gm./cc*
S_f 2	1.050
S_f 4	1.040
S_f 6	1.035
S_f 8	1.029
S_f 10	1.023
S_f 13	1.015
S_f 17	0.99
S_f 17 — S_f 40,000	(S_f 40,000 represents chylomicrons)*

* This represents a series of components with successively higher flotation rates, but so closely spaced as to be difficult of resolution as discrete components. There may be 10's or 100's of such components.

By differential preparative ultracentrifugation, individual components have been isolated (10), quite free of neighboring components, sufficiently so that the individual species can be analyzed for chemical composition. Some protein is present in all the components (from S_f 2 up to and including the chylomicrons). There is approximately 25 per cent protein in the S_f 4 species, ranging down to approximately 7 per cent protein in the S_f 40,000 (chylomicrons). Cholesterol and its esters are also present in every one of these species, from approximately 30 per cent in the S_f 4 to approximately 5 per cent in the S_f 40,000. There is a progressive shift to a higher proportion of nonesterified cholesterol in the molecules of the higher S_f classes. Phospholipid content also decreases with increasing S_f rate. Neutral fat (glyceryl esters) are prominent constituents of molecules above S_f 17, whereas they are virtually absent in those of S_f 13 and less.

Serum Lipoproteins and Atherosclerosis

Having a picture of the lipoprotein spectrum present in human serum, one may inquire as to the relation of any or all of the components to the development of atherosclerosis and related disease states. If we are to consider cholesterol in relation to such disease, it is obvious that it may be pertinent to know whether certain classes of cholesterol-bearing lipoproteins are of more importance than others may be.

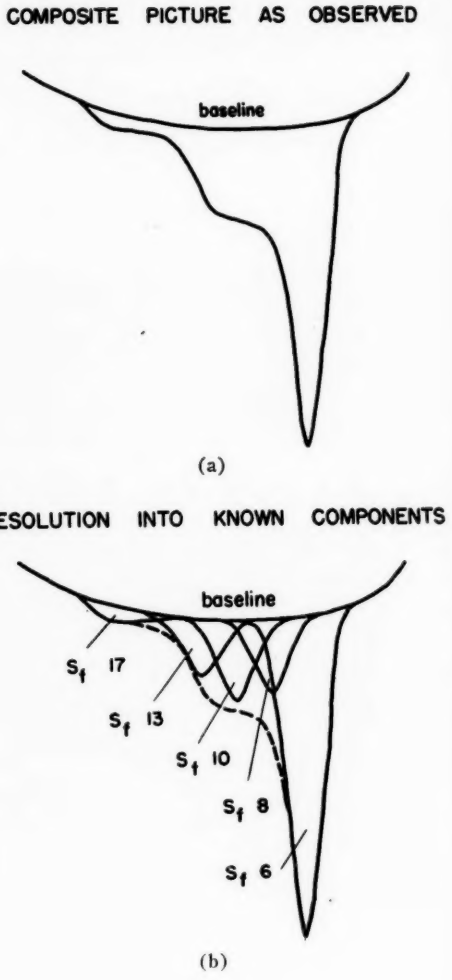


FIG. 2

(a) Diagram illustrating a typical flotation pattern observed in the ultracentrifugal analysis of the low-density lipoproteins of human serum.

(b) Resolution of 2(a) into the lipoprotein components known to exist in human serum.

The first clues that there may be differential significance to the various cholesterol-bearing lipoproteins came from a study of rabbits developing atherosclerosis as a result of cholesterol feeding (5, 6). The normal rabbit possesses only a single lipoprotein in this class at

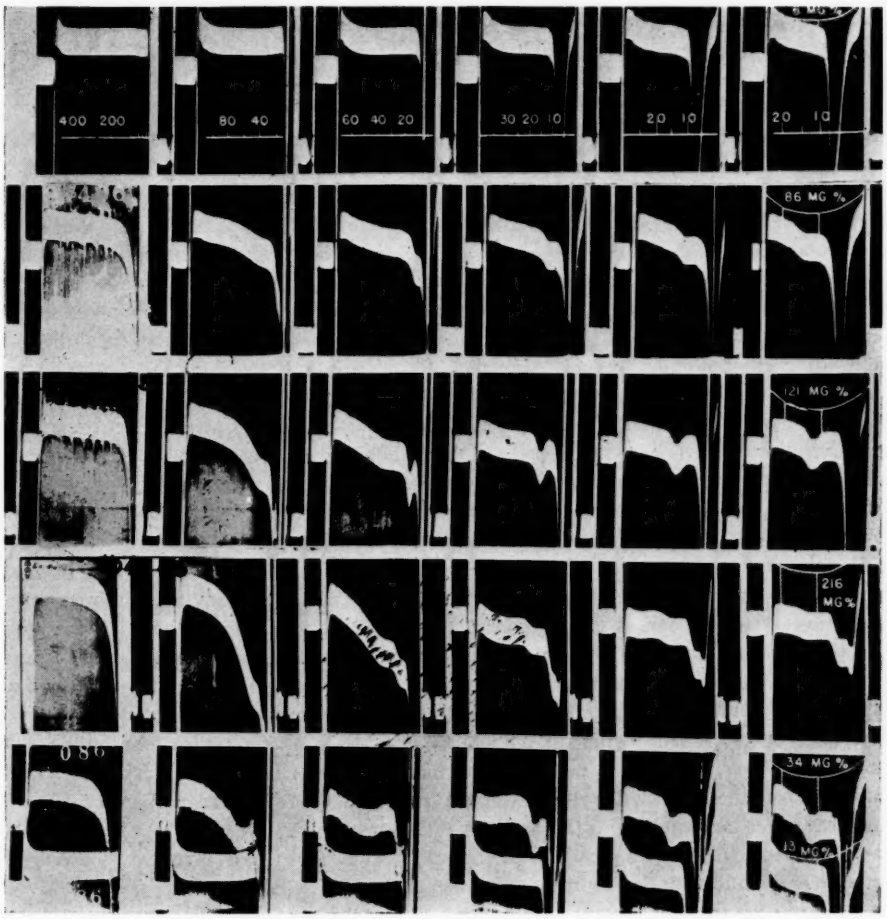


FIG. 3

(a) Flotation pattern of low-density lipoproteins from a normal 20 year old male showing exceedingly low level of S_f 10-20 molecules. Each frame is ruled for calculation of the S_f rate of any peak appearing in that frame. In this figure as well as in those below, successive frames are at 0, 6, 12, 22, 30, and 38 minutes after full rotor speed of 52,640 RPM has been reached. Hence S_f rate markings may be used on corresponding frames in all patterns below.

(b) Flotation pattern of low-density lipoproteins of a 66 year old male patient following myocardial infarction (well beyond acute phase).

(c) Flotation pattern of low-density lipoproteins of a 36 year old male with hypothyroidism subsequent to surgical therapy for Graves' disease.

(d) Flotation pattern of low-density lipoproteins of a 46 year old male with the nephrotic syndrome.

(e) and (f) Analytic flotation pattern of two different samples run simultaneously.
Upper pattern is that of a 38 year old male studied three months *before* he experienced a myocardial infarction (Note: Extremely high S_f 10-20 level Six weeks beyond the acute infarction his level was found to be 29 mg. per cent).
Lower pattern is that of a 38 year old normal female demonstrating very low S_f 10-20 level.

appreciable concentration of S_f value below 10 units. Cholesterol (or cholesterol plus oil) feeding first produces a rise in the already present S_f 10 (or less) lipoprotein. However, those rabbits developing nothing further were shown previously not to develop atherosclerosis. The majority of rabbits go beyond this during cholesterol feeding and develop components of S_f value greater than 10 units, up to several hundred S_f units.

It was also shown that one composite class, the S_f 10-30 class, shows a definite relationship to atherosclerosis in that higher concentrations of such molecules were accompanied by progressively more severe atherosclerosis, independent of the level of the S_f 10 (or less) concentration which had developed. Observations made on dogs during the procedure of experimental production of atherosclerosis by the Kendall-Steiner method of feeding thiouracil and cholesterol (8) and in the stilbesterol implantation procedure in the chicken (2) reveal similar series of components developing in these species.

In the human direct correlations of blood lipoproteins with extent of atherosclerotic activity are not so readily made for obvious reasons. However, a study of ostensibly normal individuals and those with atherosclerosis or disease states accentuating atherosclerosis do provide information linking certain of the lipoprotein molecules to development of atherosclerosis in the human.

In considering the lipoprotein pattern in evaluation of relationship to aging and disease, one is faced with the necessity of knowing something of the relative stability in level of a particular class of molecules in a single individual from day to day or with relationship to meals. Our previous studies have indicated that the levels of molecules below 20 S_f units are adequately free from fluctuation to serve as a measure of metabolic steady state, whereas for molecules of progressively higher flotation rates (greater than 20 S_f units), the blood level is influenced in relation to meals variably from individual to individual many-fold. Thus whether or not the high S_f group of molecules is related to disease, they represent a poor indicator of steady state metabolism unless some type of tolerance study is done. However, the stable character of the blood level of molecules of flotation rates below 20 S_f units renders it possible to characterize an individual in terms of his blood level of such molecules, independent of post-prandial lipemia effects.

From considerations of the data obtained in rabbits and in humans, it seems that the molecules of S_f 6 and less in the human are unlikely to be directly involved in disease production. However, the data presented previously and here indicate that the molecules between 8 S_f and 20 S_f units are of significance with respect to atherosclerosis. Ideally within this group one would like to know the relative importance of each individual species in development of atherosclerosis, information which is not yet at hand.

It does seem, however, that in the range 8 S_f units to 20 S_f units, the minor defect (if we may refer to it in this manner) is the appearance of 8 S_f molecules. Then with appreciable levels of S_f 8, the S_f 10 class may appear in appreciable concentration; when S_f 10 levels are appreciable S_f 13 molecules may be present; after S_f 13 levels become appreciable, molecules of S_f 13-20 may appear in quantity. We have never seen high levels of S_f 13-20 without appreciable S_f 13, nor high S_f 13 levels without appreciable S_f 10 levels; nor S_f 10 without S_f 8. However, all these molecules may be high *independent* of whether S_f 6 is *high or low*. Similarly in the rabbit developing atherosclerosis the molecules of successively higher S_f classes appear only after appreciable levels of the lower classes have developed.

In this discussion we are reporting all data in terms of the combined blood level of lipoproteins of the S_f 10-20 class, the S_f 10 itself being excluded. A test of the data with respect to the S_f 8-14 class reveals that similar conclusions can be drawn from this bracketing.

The obvious implication of the association of the S_f 10-30 class of molecules with rabbit atherosclerosis is that possibly these molecules themselves are those in blood transport which

ultimately provide the lipids for atheroma formation, and that the higher the blood level of such molecules the more extensive is atherosclerotic activity, given similar local factors in the arterial wall. Similarly the hypothesis is that in humans the blood level of a similar class of lipoproteins (the S_f 10-20 class) would be a reflection of the present activity of atheroma formation. Then if this hypothesis be correct, the blood levels of such molecules in various clinical categories should parallel the clinical data on atherosclerosis development in such categories. The pertinent data are presented graphically in figures 4 through 10.

(a) *"Normal" humans:* Clinically there are several outstanding features about atherosclerosis in the presumably normal population. "Presumably" is used with intent, since even with the absence of clinically manifest disease and with negative findings in a painstaking physical examination and history, extensive atherosclerosis is often present. The features of interest are:

(1) The rarity of appreciable atherosclerosis in pre-puberal children.

(2) The markedly greater incidence and severity of atherosclerosis and its serious sequelae in young adult males than in young adult females.

(3) The increase in atherosclerosis involvement in both male and female adults with aging, and the progressive obliteration of sex difference above the age of 40.

(4) The observation that autopsies of individuals dying of causes other than atherosclerotic complications reveals that a high proportion of such individuals show appreciable atherosclerosis that was not detected in the living.

Paralleling these four basic observations our measurements of S_f 10-20 lipoprotein levels in a large series of such humans reveal results completely consistent with the hypothesis that such molecules provide a measure of atherosclerogenesis.

(1) Measurements on over 50 "normal" pre-puberal children and infants (7) reveal this group to have the lowest levels of S_f 10-20 molecules of any of the normal categories. Atherosclerosis is rare in children of this age.

(2) The data in figures 4 and 5 show that

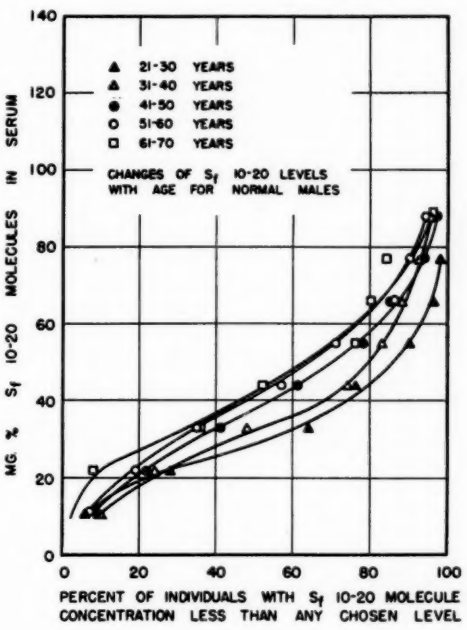


FIG. 4

Diagram illustrating the trend with age of blood levels of S_f 10-20 lipoproteins in normal males 20-70 years of age.

Notes: (1) The lipoprotein levels reported here have been revised upwards as a result of calibration changes as compared with previous data reported in reference 5. Data in figures 5 through 10 are similarly revised. The revision in no way alters the interpretations given in that reference.

(2) Data based upon 291 cases.

females in the 20 to 30 age group show consistently lower levels than males in this age group, paralleling well their lower rate of atherosclerogenesis.

(3) The data reveal a progressive rise in S_f 10-20 levels in "normals" of both sexes (at least to age 60) and a progressive diminution

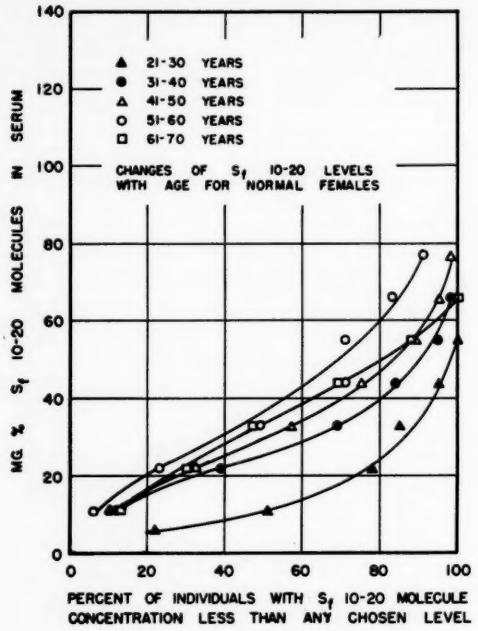


FIG. 5

Diagram illustrating the trend with age of blood levels of S_f 10-20 lipoproteins in normal females 20-70 years of age.
Note: Data based on 309 cases.

of the difference in levels between males and females, both observations being in harmony with the above-described known observations on atherosclerosis in such groups.

(b) *Living individuals with atherosclerosis:* In the absence of a clinical sequel of atherosclerosis, e.g., a myocardial infarction, we have no way of assessing clinically either the quantity of atherosclerosis present or the rate of its development. As the closest approximation to this assessment we have chosen two groups, (a) patients who have survived a myocardial infarction and (b) patients with angina pectoris who have not had an evident infarct. The basic pathology underlying both these clinical entities in the vast majority of these cases is atherosclerosis of the coronary arteries.

It is true, of course, that atherosclerosis of the coronary arteries does not necessarily measure quantitatively atherosclerosis of other vascular beds, and further that the occurrence of clinical angina pectoris or myocardial infarction does not quantitate the degree of coronary atherosclerotic involvement. Nevertheless, in the absence of a better quantitative approach, it cannot be gainsaid that a group of patients manifesting angina pectoris or a myocardial infarction will on the average be expected to have more coronary artery atherosclerosis than will a group of presumably normal individuals of similar age and sex distribution.

Figures 6, 7, and 8 show the comparison between normal people of both sexes and patients either with myocardial infarction or angina pectoris. The higher levels of S_f 10-20 molecules in these disease categories (being primarily on an atherosclerotic basis) than in cor-

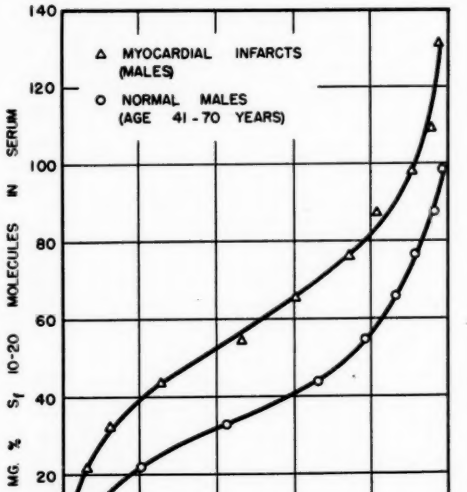


FIG. 6

Diagram illustrating the higher levels of S_f 10-20 molecules in males with myocardial infarction than in normal males of corresponding ages.
Notes: (1) All patients with infarction were at least 6 weeks beyond infarction date.
(2) Data based on 203 myocardial infarcts and 241 normal males.

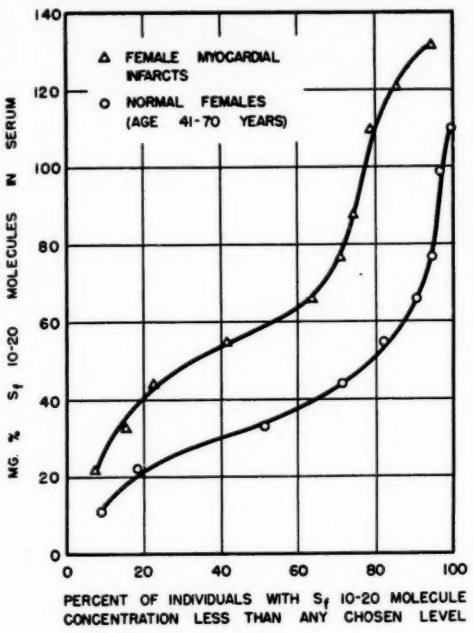

FEMALE MYOCARDIAL INFARCTS
NORMAL FEMALES (AGE 41-70 YEARS)
MG. % Sf 10-20 MOLECULES IN SERUM
PERCENT OF INDIVIDUALS WITH Sf 10-20 MOLECULE CONCENTRATION LESS THAN ANY CHOSEN LEVEL

FIG. 7

Diagram illustrating the higher S_f 10-20 levels in females with myocardial infarction than in normal females of corresponding ages.

Notes: (1) All patients with infarction were at least 6 weeks beyond infarction date.
(2) Data based on 27 female myocardial infarcts and 139 normal females.

responding normal people, for all ages and both sexes, provide a strong link in the chain of evidence implicating this class of molecules in the development of atherosclerosis in humans.

The data as presented in figures 6, 7, and 8 allow one to compare normal people with the coronary disease patients at any level of S_f 10-20 molecules, e.g., at a level of 25 mg. per cent, 26 per cent of normal males are below this level whereas 9 per cent of patients with cardiac infarct are. Or, at the higher levels, one sees that at a high level of 80 mg. per cent 22 per cent of males with myocardial infarction are above this level, but only 7 per cent of normal people are. Thus three times as many infarct patients have such high levels as do normals.

That *some* normal people have levels higher than many patients with clinically evident coronary artery disease is not surprising or unexpected. Indeed it would be inconsistent that they should not, since it is highly reasonable to assume that such normal individuals are developing atherosclerosis, provided local factors are appropriate, but have simply not yet had a clinical sequel. After all, the occurrence of a myocardial infarction is simply a mechanical hazard along the course of evolution of atherosclerotic disease, and atherosclerosis can be full-blown without such a manifestation. That a *small* proportion of patients with angina or myocardial infarction show low S_f 10-20

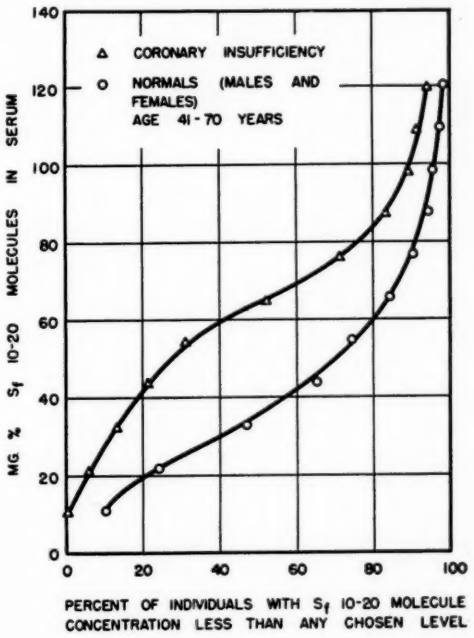

CORONARY INSUFFICIENCY
NORMALS (MALES AND FEMALES) AGE 41-70 YEARS
MG % Sf 10-20 MOLECULES IN SERUM
PERCENT OF INDIVIDUALS WITH Sf 10-20 MOLECULE CONCENTRATION LESS THAN ANY CHOSEN LEVEL

FIG. 8

Diagram illustrating the higher S_f 10-20 levels in patients with coronary insufficiency (as manifested by angina pectoris) than in normals.

Notes: (1) No significant differences were found between the males and females in these groups, so the plots are composite for both sexes.
(2) Data based on 63 patients with coronary insufficiency and 380 normals.

levels is not unexpected. A few of such patients may have a nonatherosclerotic basis for their disease. Others may well have had high levels of such molecules before the infarction with a subsequent drop due to dietary and drug manipulation subsequent to the clinical episode.

Such a case in point is that of a 38 year old male we studied first as normal. At that time his S_f 10-20 level was 134 mg. per cent (fig. 3e). Several months later he experienced a myocardial infarction and was treated with usual measures plus dietary restriction. His blood level at the sixth week after the episode was down to 29 mg. per cent. However, had we not known from several premyocardial infarction studies that he had carried an exceedingly high level of such molecules, he might erroneously have appeared to be an exception to the rule of elevated S_f 10-20 lipoprotein levels accompanying atherosclerosis.

Hypertension, S_f 10-20 Lipoproteins, and Atherosclerosis

The frequency with which hypertensive patients suffer coronary artery occlusions and the generally accepted clinical evidence of excessive atherosclerosis in many hypertensive patients both suggest that hypertension may predispose to atherosclerosis. Many have suspected that the elevated pressure per se is the responsible factor in accentuating atherosclerosis. Yet it is well known that some patients with severe hypertension (in terms of actual pressure levels) come to autopsy with minimal atherosclerosis.

In an effort to evaluate the factors in hypertensive subjects responsible for excessive atherosclerosis we have made a comparison of 139 patients suffering from essential hypertension without known complications, studied because of their hypertension itself, with 95 cases of myocardial infarction and/or coronary insufficiency who happened also to have elevated diastolic pressures (100 mm. diastolic minimum used for these purposes). The data,

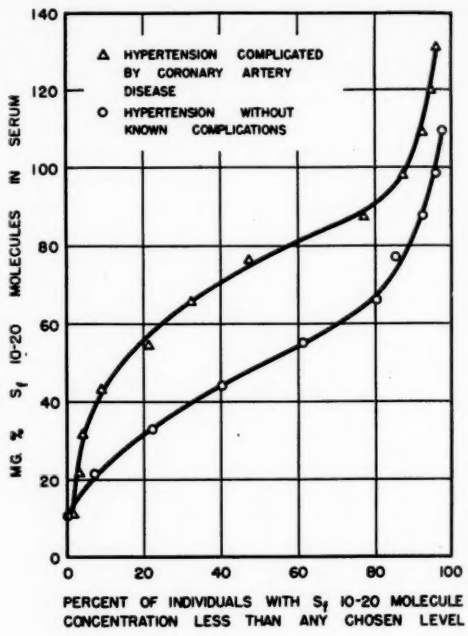


Fig. 9

Diagram illustrating the higher S_f 10-20 lipoprotein levels in hypertensives complicated by coronary artery disease than in hypertensives without such known complications.

Notes: Based on 95 hypertensives with known coronary artery disease and 139 hypertensives without known coronary disease. (Age group 41-70 years).

presented in figure 9, show that hypertensive patients who have such a demonstrable manifestation of atherosclerotic disease have a much higher frequency of high S_f 10-20 lipoprotein levels (and higher average levels) than do individuals with uncomplicated hypertension.

Since blood pressures were not appreciably different in the two groups, it would appear that a primary factor which resulted in atherosclerotic manifestations in the hypertensive patients who also have demonstrable coronary artery disease may be their elevated S_f 10-20 lipoprotein levels as compared with the uncomplicated hypertensive group. Further, the existence of appreciable numbers of hyper-

tensive patients without evident atherosclerotic complications who have relatively low S_f 10-20 levels in spite of long duration of severe blood pressure elevations may explain the clinical observation that an appreciable segment of the hypertensive population survives a long period without developing clinical sequelae of atherosclerosis.

Diabetes Mellitus, S_f 10-20 Lipoprotein Levels, and Atherosclerosis

The known frequency of severe atherosclerotic complications in diabetes mellitus provides probably the most serious problem existing in the management of the diabetic patient. In the effort to evaluate the factor responsible for excessive hypertensive or atherosclerotic vascular disease in diabetes mellitus, we have compared a series of diabetic patients between 40 and 70 years of age, as yet uncomplicated by clinically evident vascular disease, with another series of diabetic individuals already demonstrating hypertension and/or coronary artery disease.

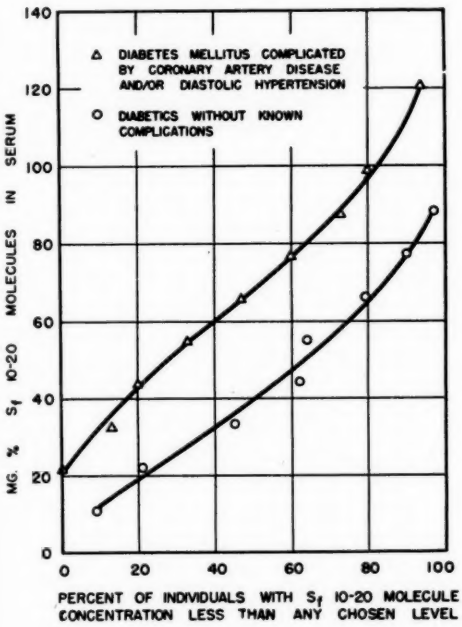


Fig. 10

Diagram illustrating the higher S_f 10-20 lipoprotein levels in diabetics complicated by hypertension and/or coronary artery disease than in diabetics without such known complications.

Note: Data based on 15 diabetics with vascular complications and 58 diabetics without such known complications. (Age group 41-70 years).

The data presented in figure 10 show that the patients with diabetes already manifesting such vascular disease show strikingly higher S_f 10-20 lipoprotein levels than do diabetic individuals without such complications. This would implicate the level of such molecules as a major factor, at least, in the development of vascular complications in diabetes mellitus, and further may shed some light on the ability of a certain proportion of middle-aged diabetic patients to live with their disease many years without encountering serious complications of atherosclerosis.

S_f 10-20 Lipoprotein Levels in other Diseases Associated with Excessive Atherosclerosis

Several clinical entities, including myxedema, xanthoma tuberosum, and nephrosis, are known to predispose to premature and excessive atherosclerosis.

a. *Myxedema:* Twelve patients with hypothyroidism or frank myxedema have been studied with respect to S_f 10-20 lipoprotein levels (fig. 3c). In all cases very high S_f 10-20 lipoprotein levels were observed (average level 132 mg. per cent). Some of these patients showed levels in the 200 mg. per cent range which are far higher even than the majority of patients with vascular disease. A few patients with treated myxedema studied initially after therapy with thyroid extract showed much lower levels, suggesting that the thyroid therapy may have reduced their levels. This possibility is strengthened by our own observations in a small series of hypothyroid patients being followed who are demonstrating drops in S_f 10-20 levels on thyroid extract.

An evaluation of thyroid extract in apparently euthyroid individuals is in progress. In two children with thyroid carcinoma in whom hypothyroidism was being artifically induced by Farr and Robertson, classical lipoprotein patterns of the hypothyroid state were observed with the S_f 10-20 level being greatly elevated.

b. *Xanthoma tuberosum:* Four patients with classical xanthoma tuberosum have been studied(12). The greatly increased atherosclerosis in such patients is well known. All 4 patients in this category showed fantastic S_f 10-20 lipoprotein levels in their sera, without striking elevations in the level of the S_f 6 and lower molecules, indicating that their abnormality is not simply increased levels of all cholesterol-bearing molecules, but rather only of those in special classes.

c. *Nephrosis:* Ten patients manifesting the nephrotic syndrome showed uniformly high S_f 10-20 levels, some with and some without appreciable elevations of the S_f 6 and lower classes of lipoproteins (fig. 3d).

The exceedingly high S_f 10-20 lipoprotein levels in these three disease categories, myxedema, xanthoma tuberosum, and nephrosis, generally with S_f 6 cholesterol-bearing lipoproteins in the normal range, suggests strongly that the S_f 10-20 class of lipoproteins is more associated with the excessive atherosclerosis of these diseases than is the hypercholesterolemia often accompanying them.

The Relationship of S_f 10-20 Lipoprotein Levels to Total Blood Cholesterol

We have pointed out previously (5, 6) that molecules of the S_f 10-20 class may be present at high levels in a particular patient's blood no matter whether the blood cholesterol is high, low, or intermediate. More extensive studies have completely confirmed this observation.

Since the blood cholesterol (either free or esterified) exists in the form of several different lipoproteins, it is apparent that a priori one cannot predict that the relative proportions of the several lipoproteins will remain the same at various levels of total blood cholesterol. In fact, the opposite is often true, so that in one serum the ratio of S_f 10-20 molecules to S_f 6 molecules may be high, whereas in another serum with a much higher total cholesterol level the ratio of S_f 10-20 molecules to S_f 6 may be quite low. So great are these variations that the total blood cholesterol level is valueless in predicting the S_f 10-20 level in a particular patient.

While it is true that in general the S_f 10-20 level rises with elevation in blood cholesterol, the deviations from this rule are so frequent and severe that one would be grossly deceived by the use of the total blood cholesterol as an indicator for the presence of these particular S_f 10-20 molecules. Further, the frequent occurrence of high S_f 10-20 lipoprotein levels with low total blood cholesterol (even below 150 mg. per cent total) would indicate that in evaluation of atherosclerotic potentialities a low serum cholesterol may be highly deceptive in predicting the absence of the possibly noxious S_f 10-20 molecules.

An appreciable fraction of blood cholesterol is often in the S_f 6 lipoprotein. Such sera may have exceedingly low levels of the S_f 10-20 class, a condition which is found especially frequently in the sera of children and young adult females. Since these groups show very little atherosclerosis and since numerous patients with manifest atherosclerosis show much lower S_f 6 levels but high S_f 10-20 levels, we, tentatively at least, are of the opinion that the S_f 6 molecule per se is not involved in atherosclerogenesis.

The common presence of S_f 10-20 molecules in sera from patients with manifest atherosclerosis, or with diseases predisposing thereto, independent of the level of total serum cholesterol, may aid in explaining the dissatisfaction held by many clinicians over the apparent failure of blood cholesterol levels to correlate well with atherosclerotic activity.

Recently much attention has been paid to cholesterol-phospholipid ratios as indices of atherosclerotic activity (1). Just as with serum

cholesterol, the cholesterol-phospholipid ratios can only be satisfactorily interpreted in the light of the knowledge of which of various cholesterol- and phospholipid-bearing lipoproteins are present in a particular serum.

Since from studies (10) on isolated lipoproteins from human serum it appears that the entire group of low density lipoproteins (S_f 4—S_f 100) show weight ratios of cholesterol to phospholipid of 1.0 to 1.4, whereas the high density lipoproteins (3) (a group not treated in this paper) show ratios in the neighborhood of 0.45, the aggregate total cholesterol to phospholipid ratio will depend upon the relative abundance of low and high density lipoproteins much more than upon the distribution among the low density lipoproteins, e.g., between the S_f 6 and S_f 10-20. Thus a person might have a low phospholipid-cholesterol ratio due to a high S_f 6 level relative to the level of the high density lipoprotein group. From the low phospholipid-cholesterol ratio, some workers might predict a likelihood of high atherosclerotic activity, whereas from the absence of appreciable S_f 10-20 levels we would be led to just the opposite conclusion.

The evidence that suggests that low phospholipid-cholesterol ratios are common in atherosclerotic patients probably results from the frequent occurrence of high levels of all the lipoproteins of the S_f 3-100 class in such patients. However, the phospholipid to cholesterol ratio fails to distinguish between the various components of the S_f 3-100 class, since all these components have approximately the same phospholipid-cholesterol ratios. Thus a patient with a high total S_f 3—S_f 100 class, but a low S_f 10-20 level, would be considered as high in atherosclerotic activity by some workers whereas we would consider such an individual as low in this respect.

Again, a patient with a high S_f 10-20 level might have a low total S_f 3-100 level but a high level of high density lipoproteins with its concomitant high phospholipid-cholesterol ratio. Such a total serum might have a high phospholipid-cholesterol ratio, indicating low atherosclerotic activity. We would consider just the opposite to be true.

Modification of the Blood Levels of the S_f 10-20 Class of Lipoproteins

The hypothesis that such molecules as the S_f 10-20 class of lipoproteins may be the source of lipids in atheromata renders it of obvious potential prophylactic and therapeutic interest to understand the factors which may modify these levels. Changes produced by administration of thyroid extract in certain selected patients and caused by the combination of features attendant upon a myocardial infarction in the acute phase have already been mentioned above.

As previously reported (5, 6) we have been investigating the effect of a low fat—low cholesterol dietary regimen both in a controlled hospital dietary group and in ambulatory patients at home. The cumulative evidence indicates that appreciable reductions in S_f 10-20 levels are obtainable by the use of a diet containing 20 to 50 gm. of total fat, restricted in cholesterol to approximately 200 mg. per day, but adequate in protein. The allowance of vegetable fats to 100 gm. in patients previously restricted in total fats to 20 gm. results in general in a rise of S_f 10-20 levels. Thus the restriction of both animal and vegetable fats is required, independent of cholesterol intake. The results obtained in the hospital controlled series indicate that weight loss or weight gain did not appear to influence responses, since even with maintenance of weight to within ± 3 pounds changes in the lipoproteins occurred with changes in dietary fats and cholesterol.

The changes in levels of S_f 10-20 molecules (and in those of the S_f 8-10 class) observed in dietary restriction may or may not be accompanied by appreciable changes in total serum cholesterol. Thus a two-fold lowering of lipoprotein levels may be observed with a much lower percentage alteration in serum cholesterol level. This should be understandable in the light of the preceding discussion concerning the numerous types of cholesterol-

bearing molecules present in serum. The fact that serum cholesterol may not drop appreciably by dietary cholesterol reduction has probably been the source of discouragement in the clinical application and evaluation of efficacy of such dietary restriction in atherosclerosis. However, twofold drops in S_f 10-20 lipoprotein levels seen in dietary restriction even without large concomitant serum cholesterol drops render such evaluation essential.

Dietary response is variable from individual to individual, some showing very little response to 35 to 50 gm. fat diets at home. It must, however, always be considered that until such apparently refractory patients have been tested under controlled conditions one cannot truly claim the patient to be refractory. The advertent and inadvertent errors in dieting by the patient eating at home are discouragingly frequent. Further, the necessity for careful instruction concerning what a low fat diet really means is frequently overlooked. It is more important that the patient know what he can eat rather than merely what he cannot eat. It is yet too early to make any definite statement as to clinical efficacy of such dietary restriction.

Interrelationships Among the Various Lipoproteins

An ultimate understanding of the mechanism of maintenance of the blood levels of the various lipoproteins is obviously the goal which is to be striven toward in the effort to gain an insight into the nature of the defect which results in abnormal elevations of such molecules as the S_f 10-20 class in certain individuals. All the serum lipoproteins should be regarded as in transit, the steady state blood levels of any particular molecule being the result of balance between rates of influx of that molecule into serum and its rate of disappearance from serum to whatever sites of ultilization, storage, or destruction. Hormonal influences obviously suggest themselves from such observations as the male-female differences in levels, from abnormal and often very high S_f 10-20 levels seen in the pregnant female (11) as contrasted with the nonpregnant female of the same age whose levels are generally very low.

Certain patterns are becoming clarified as to interrelationships of the various molecular levels. Those individuals with low levels of S_f 10-20 lipoproteins generally, although not always, show very low levels of all the lipoproteins in the S_f 20-100 class as well (fig. 3a). Individuals who show high levels of S_f 10-20 molecules (and also S_f 8-10) quite often show in addition appreciable levels of the lipoproteins of the S_f20-100 class. On the other hand, in some patients very high S_f 10-20 levels are observed without accompanying high levels of molecules of S_f 20-100. The S_f 30-100 class of molecules is acutely influenced (in matters of hours) following high fat meals, but to a variable degree in different individuals.

It would appear that the defect involved in the maintenance of high levels of these S_f 10-20 molecules, which are related to atherosclerosis, represents one facet of what may be a general disturbance in the overall metabolic pattern of handling fats and cholesterol, at least in so far as the blood transport mechanism is concerned. A more penetrating understanding of this disturbance requires further clarification of the interrelationships, source, and site of removal of all the various classes of lipoproteins involved.

Summary

1. Serum lipid transport is describable in terms of a group of lipoprotein macromolecules of differing physical properties and chemical composition. Certain of these lipoproteins (the S_f 10-20 class—and the S_f 8-10 class) are associated with human atherosclerosis.

2. While total serum level of any one of the lipid constituents, e.g., cholesterol or phospholipids, is determined by the presence and amount of the individual lipoprotein molecules, the converse is not true. Thus the serum total cholesterol is of no value in predicting the

level of the S_f 10-20 class of lipoproteins for any particular individual.

3. Patients with myocardial infarction or angina pectoris show consistently higher levels of such molecules than do apparently normal individuals.

4. Hypertensive patients who have coronary artery disease (presumably atherosclerotic in origin) show higher S_f 10-20 levels than do individuals with uncomplicated hypertension.

5. Diabetic patients with vascular disease (hypertension and/or coronary artery disease) show higher levels than do diabetic individuals who do not show these complications.

6. Dietary restriction of total fats plus cholesterol slowly reduces the level of S_f 10-20 molecules, the extent and rate of reduction being variable from patient to patient.

7. The presence of the S_f 10-20 class of molecules in high concentration is noted in such diseases as myxedema, nephrosis, and xanthoma tuberosum where atherosclerosis is excessive.

8. The factors influencing the level of S_f 10-20 lipoproteins and the observed relationships to other lipoproteins of serum suggest a general metabolic disorder in fat and cholesterol transport associated with the presence of this particular group of molecules that are involved in atherosclerosis.

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References

1. Ahrens, E. H., Jr.: The Lipid Disturbance in Biliary Obstruction and Its Relationship to the Genesis of Arteriosclerosis. *Bull. New York Acad. Med., 26:* 151-162, 1950.
2. Chaikoff, I. L., Gofman, J. W., Lindgren, F. T. Jones, H. B.: Ultracentrifugal Studies of the Lipoproteins in Chicken Atherosclerosis Induced with Stilbesterol. To be published.
3. Elliott, H. A., Perks, M., Gofman, J. W., Jones, H. B., Lindgren, F. T.: The High Density Lipoproteins of Human Serum. To be published.
4. Gofman, J. W., Lindgren, F. T., Elliott, H. A.: Ultracentrifugal Studies of Liproproteins of Human Serum. *J. Biol. Chem., 179:* 973-979, 1949.
5. Gofman, J. W., Jones, H. B., Lindgren, F. T., Lyon, T. P., Elliott, H. A., Strisower, B.: Blood Lipids and Human Atherosclerosis. *Circulation, 2:* 161-178, 1950.
6. Gofman, J. W., Lindgren, F. T., Elliott, H., Mantz, W., Hewitt, J., Strisower, B., Herring, V.: The Role of Lipids and Lipoproteins in Atherosclerosis. *Science, 111:* 166-171, 1950.
7. Kempe, H., Silver, H., Gofman, J. W.: The Lipoproteins of Serum in Infancy and Childhood. To be published.
8. Kendall, F. E., Davidson, J., Gofman, J. W., Jones, H. B., Lindgren, F. T.: Ultracentrifugal Studies of the Lipoproteins in Dogs Developing Atherosclerosis. To be published.
9. Lindgren, F. T., Elliott, H. A., Gofman, J. W.: Ultracentrifugal Characterization and Isolation of Human Blood Lipids and Lipoproteins. *J. Phys. and Colloid Chem., 55:* 80-93, 1951.
10. Lindgren, F. T., Nichols, A., Freeman, K., Gofman, J. W., Jones, H. B.: Chemical Characterization of the Lipoproteins of Human Serum. To be published.
11. Lyon, T. P., Borson, J., Elliott, H. A., Page, E., Gofman, J. W.: The Serum Lipoproteins in Pregnancy. To be published.
12. McGinley, J. P., Gofman, J. W.: Ultracentrifugal Studies of Serum Lipoproteins in Xanthoma Tuberosum. To be published .

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Assessment of Physiologic Age by Combination of Several Criteria—Vision, Hearing, Blood Pressure, and Muscle Force

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It is well known that chronologic age is not necessarily the same as physiologic age. Physiologic age implies an assessment of the functional capacities of an individual by reference to standards derived from healthy persons of the same chronologic age as the person who is being tested. It is of course necessary to choose such physiologic functions that change demonstrably with chronologic age.

Various observers have demonstrated relationships between age and the following physiologic functions:

1. Range of visual accommodation—reduced with age (1, 7).
2. Auditory acuity—reduced with age (3, 4).
3. Systolic blood pressure—increased with age (10, 12).
4. Sensitivity of the dark-adapted eye—reduced with age (2, 5, 11).
5. Hand grip—strength reduced with age (6, 16).

Because these physiologic functions are not closely related to each other and because they vary in their rate of aging, no one function would give an adequate index of physiologic age.

It seems reasonable to assume that a method that would in some way combine the various physiologic functions would give a more useful assessment of the individual. Assessment of aging in the individual as a biologic unit, however, cannot be made on physiologic functions alone, but by combining them with anatomic and psychologic observations. Such a method would give an assessment of biologic rather than physiologic age.

The investigation here reported represents an effort to discover a method of combining the foregoing five physiologic criteria—a method that could be extended to incorporate as many criteria as might be desired.

Material and Methods

Thirty-eight men, aged 21 to 84 years, from business and professional classes, including 4 university students, formed the major part of an exploratory x-ray survey of age changes in bones and joints now being carried out in the Dalhousie University Anatomy Department. As part of the survey, the five physiologic functions mentioned above were tested. The men were originally selected so that the ages would be fairly evenly scattered through the third to the eighth decade.

Detailed clinical histories of all subjects were recorded and serologic reactions of the blood for syphilis were all negative. It was, however, impracticable to make a thorough clinical examination of each subject because most of the men were members of the public who had generously volunteered for several time-consuming attendances in the x-ray division of the Anatomy Department. Therefore the term "healthy" as applied to them would mean "symptomless." (One subject had been under treatment for prostatic cancer four years previously.) For this reason and also because the sample was too small and not representative of the social and occupational classes of the population, it should not be assumed that the figures that will be given later represent a standard. Their purpose is merely to illustrate a method by which standards may be found.

Tests

All the tests on all subjects were conducted by the writer, and the subjects were called in

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for testing in strictly random order, as determined by a table of random numbers.

Range of visual accommodation.—Instrument: Prince's rule and a Snellen's test type card. Procedure: One end of the rule was placed against the cheek below one eye, while the other eye was completely covered. The test card, attached to the rule by a sliding mechanism, was moved toward the eye until a point was reached where the print became blurred. The distance (in centimeters) from the cheek to the test card was recorded as the subject's near point. The card was then moved along the rule away from the eye until the same type again became blurred. This distance on the rule from the cheek to the test card was recorded as the subject's far point. The range of accommodation was recorded as the average range of both eyes.

Auditory acuity.—Instrument: Maico audiometer, model D-9. Procedure: Air conduction was tested in each ear over 11 frequencies from 64 to 11,584 cycles per second. At each frequency a reading was made of the minimum intensity (in decibels) at which the subject could hear the sound. As is customary, the difference between this reading and zero decibels was taken to represent the loss in auditory acuity. This loss was summated for all frequencies in each ear and the average of both sums was found.

Systolic blood pressure.—Instrument: Mercury sphygmomanometer. Procedure: Blood pressure determinations were always made 25 to 30 minutes after the subject's x-ray examination of bones and joints. Systolic and diastolic blood pressure readings were made from the left arm with the subject in the sitting position. A second reading was made after a similar x-ray procedure two to three weeks later. The average of the two systolic readings was used as the subject's systolic blood pressure.

Sensitivity of the dark-adapted eye.—Instrument: Crookes' adaptometer, model No. 8. Procedure: Each subject was seated in a completely dark room for thirty-five minutes before the test. Following this period of dark adaptation the subject faced the test object (an arrow of light) a constant distance (two feet) from his eyes. The brightness of the test object was gradually reduced by means of neutral density filters and crossed polaroids until a point was reached when the subject was unable to orientate the test object. Binocular vision was used for the test and the actual time of testing was ten to fifteen minutes. Brightness was measured in micro-microlamberts and the subject's final threshold reading was taken forty-five to fifty minutes from the beginning of dark adaptation. Subjects with visual acuity under 20/60 were corrected for the test, and the loss of light by reflection and absorption of the lenses, approximately $10^{0.05}$ micro-microlamberts, was subtracted from the final threshold.

Hand grip.—Instrument: Collin's hand dynamometer. Procedure: The strength of hand grip measured in pounds was found for right and left hands. The average measurement of both hands was taken as the subject's strength of hand grip.

Physiologic Function Corresponding to Age

The relationship between physiologic function and chronologic age is commonly presented by expressing values of the function at different ages. The usual way of doing this was exemplified by Ulfland's (16) statement of mean strength of hand grip for adults in each

decade above 20 years. A more satisfactory form is an equation showing regression of physiologic function on age—a standard statistical procedure, which however, is seldom found in gerontologic literature.

Sometimes a correlation coefficient is given; for example, Robertson and Yudkin (11) found the coefficient of correlation between age and final rod threshold to be +0.56. This, being significant, shows that the relationship can to some extent be expressed as a straight line, but it does not make allowance for curvilinearity which in many published graphs appears very obvious.

On the 38 men the following coefficients of correlation with age were found for each of the five physiologic functions:

	r
Range of visual accommodation	—0.7587
Loss of auditory acuity	+0.8290
Systolic blood pressure	+0.4834
Visual threshold of the dark-adapted eye	+0.7203
Strength of hand grip	—0.6621

All coefficients are highly significant ($P < 0.01$). Fisher's test of significance (8, sect. 35) showed that there was no significant difference between the coefficient 0.7203 and Robertson and Yudkin's coefficient of 0.56 mentioned previously. Chieffi and Kirk (5) observed a coefficient of +0.41 between age and adaptation time. No coefficients were found in the literature for comparison with the others in the foregoing list.

To display curvilinearity of regression (8, sect. 25) an equation was found for each of the five physiologic functions. Each equation contained age and the square of age, and in no instance did the cube of age give a significantly better fit. The regression equation showing the relationship between range of visual accommodation and age was:

$$Y = 7.5646 - 0.3982\ (a_1 - 3.4658) + 0.00052005\ (a_2 - 327.6897).$$

The actual values of the ages and the physiologic functions, when squared and cubed, proved too unwieldy even for a calculator that would take ten-figure numbers. For this reason the ages and the values for all the physiologic functions, with the exception of sensitivity of the dark-adapted eye, were coded, i.e., reduced by an appropriate amount.

In the above equation the dependent variate Y = range of visual accommodation (cm. — 20); a_1 = age (years — 50); $a_2 = (a_1)^2$; mean observed value for range of accommodation = 7.5646 (cm. — 20); standard error of the estimate = 6.3218 cm.

For each individual the departure from expected physiologic function (Y) was found as in the following example: Subject No. 1.— Y = —5.4089 (cm. — 20); actual range of accommodation = —9.50 (cm. — 20); difference / S.E. of estimate = +4.09/6.3218 = +0.647. By convention a plus sign was used to indicate that the observed range of accommodation was appropriate to an older person, a minus sign the opposite. The same procedure was followed for each of the five functions and therefore each subject had five ratios.

It will be recalled that the object of the investigation was to find a method of combining the assessments and therefore the question was: Would one be justified in summating these ratios for assessment of physiologic age? This would, however, imply the assumption that all the physiologic functions should have equal weight in determining physiologic age and there is no basis for such an assumption. Alternatively, if blood pressure should receive greater weight than hand grip, the question would be: How much greater weight?

There is another objection to the use of these individual equations, namely, that they do not eliminate the possibility of interrelationships between the various physiologic functions. If, for example, there were a relationship between blood pressure and hand grip due to the effect of a more adequate blood supply to a muscle, an increased strength of hand grip might re-

sult. In the expression derived from hand grip there would be included some effects of blood pressure.

For these reasons the method was not pursued further and attention was turned to another method of expressing the relation of age to physiologic function.

Age Corresponding to Physiologic Function

The type of equation required was one that would eliminate possible interrelationships between the various physiologic functions and at the same time give each function its proper weight. The equation that would best meet these specifications was a multiple regression equation (13, sect. 13.12) combining the five physiologic functions.

$$\begin{aligned} Y = 3.465789 &- 0.155269(x_1 - 6.355263) \\ &- 0.0153716(x_2 - 127.1250) \\ &+ 76.686385(x_3 - 3.485526) \\ &- 9.321200(x_4 - 12.283882) \\ &+ 1.268605(x_5 - 1.154474) \\ &- 0.0405237(x_6 - 94.656666) \\ &+ 0.0362998(x_7 - 2.355263) \\ &- 0.00321828(x_8 - 328.822368) \\ &- 0.122417(x_9 - 6.513158) \\ &+ 0.00170118(x_{10} - 310.006579) \end{aligned}$$

Y = estimated physiologic age (years — 50).
x_1 = range of visual accommodation (centimeters — 20); $x_2 = (x_1)^2$.
x_3 = threshold of the dark-adapted eye (micro-microlamberts); $x_4 = (x_3)^2$.
x_5 = loss of auditory acuity (decibels — 20); $x_6 = (x_5)^2$.
x_7 = systolic blood pressure (millimeters of mercury — 130); $x_8 = (x_7)^2$.
x_9 = strength of hand grip (pounds — 50); $x_{10} = (x_9)^2$.

The mean observed age was +3.465789 (years — 50), i.e., 53.465789 years.

The physiologic age of each subject was calculated from this equation and the differences between physiologic and chronologic ages are shown in table 1. (The numerous decimal figures, carried up to this stage to avoid risk of gross error, could now be eliminated.)

By convention a minus sign indicates that a subject was younger, by estimated physiologic age, than was indicated by the calendar; a plus sign indicates the reverse.

In table 1 the number of negative differences is 20 and the number of positive differences is 18. It seems as if there might be an excess of negative values among the older men, but when the men were classified with age 50 as arbitrary dividing line, the distribution was:

	Over 50	Under 50	Total
Negative	13	7	20
Positive	9	9	18

From tables of binomial confidence limits (9) it can be shown that 7 out of 20 is not a significant minority; and a chi square test showed no significant difference in proportions of negative and positive values between the two age groups.

A more sensitive test of the randomness of any observed grouping of consecutive positive and negative deviations (14) indicated that the grouping of negative and positive differences throughout the whole series, as well as in the groups above and below 50 years, could be accounted for by chance. Therefore, as far as could be shown, the equation was equally applicable at all age periods.

In this series of men the standard error of estimated physiologic age was ± 7.35 years. Taking the usual confidence limits of twice the standard error, a man would not be judged physiologically older or younger unless his physiologic age differed by more than ± 14.7 years from his chronologic age.

If many more physiologic, anatomic, and psychologic criteria with a larger number of subjects were used, a smaller variation might be found, but it is quite possible that adults do vary as much as this, i.e., that different

TABLE I. COMPARISON OF CHRONOLOGIC AND PHYSIOLOGIC AGES.

SUBJECT NO.	PHYSIOLOGIC AGE (P)	CHRONOLOGIC AGE (C)	DIFFERENCE (P-C)
1	79.4	84.1	− 4.7
2	70.8	77.0	− 6.2
3	71.0	73.3	− 2.3
4	69.6	73.2	− 3.6
5	62.3	72.6	−10.3
6	71.3	70.8	+ 0.5
7	66.4	71.1	− 4.7
8	72.9	70.5	+ 2.4
9	68.5	68.9	− 0.4
10	68.4	69.1	− 0.7
11	65.1	67.2	− 2.1
12	66.700	66.715	− 0.015
13	54.9	70.7	−15.8
14	62.3	66.4	− 4.1
15	74.6	64.6	+10.0
16	70.6	64.3	+ 6.3
17	71.1	60.1	+11.0
18	61.8	59.5	+ 2.3
19	54.9	58.4	− 3.5
20	64.9	57.8	+ 7.1
21	61.0	57.0	+ 4.0
22	53.8	52.9	+ 0.9
23	43.7	45.6	− 1.9
24	44.9	44.4	+ 0.5
25	41.5	44.7	− 3.2
26	40.0	43.8	− 3.8
27	34.7	40.2	− 5.5
28	30.5	40.7	−10.2
29	32.7	38.6	− 5.9
30	38.5	36.7	+ 1.8
31	48.4	35.4	+13.0
32	39.9	34.6	+ 5.3
33	34.4	32.7	+ 1.7
34	25.7	28.9	− 3.2
35	24.7	24.5	+ 0.2
36	29.9	22.1	+ 7.8
37	26.7	21.3	+ 5.4
38	32.6	21.3	+11.3

healthy persons differ to this extent in their rates of aging.

As with most biologic phenomena, the true distribution above and below the expected values would probably be skewed. Instead of using a multiple of the standard error, therefore, the percentile method of recording variation would be desirable, as it is used in assessment of body weight (15).

In the equation used here, the squares of the physiologic functions were introduced because graphs suggested a curvilinear relationship. In this preliminary survey, no higher powers were used because even with squares the computation was beyond the ordinary limits of the calculating machine.

In any large-scale investigation for assessment of aging, it would be necessary first of all to express age in terms of each physiologic function separately, using the square, cube, and

higher powers of the function to make the best estimate for each age. When this had been done, the physiologic functions with their squares or appropriate higher powers would be combined in a multiple regression equation as shown previously. Age, the dependent variate, would have to be unselected.

Suggestions for Future Investigations

The weakness of the multiple regression method as employed in the present investigation arises from the fact that the men were selected so as to provide a fairly equal number in each decade, and "a selection of the dependent variate may change the regression line altogether" (8, sect. 25).

Therefore in order to obtain a regression equation applicable to a particular population, a random sample of that population would be necessary. It is obviously impossible to get a random sample of the general population. Such samples are sometimes obtained from large industrial groups and the question would be: If standards were based on a survey of such group, would one be justified in applying these standards when assessing age in the general population? One important objection is that, in industrial groups, few people are found over the age of 65 years. Another objection is that prematurely aged subjects in industry tend to leave for less strenuous occupations. Standards obtained from a survey of such a group, therefore, would only be applicable to similar industrial groups.

Random samples taken from policy-holders of life insurance companies may be more representative of a large section of the general population than samples of any other specific group. Standards for the assessment of aging obtained from such a survey could be applied to applicants for life insurance, and standards derived from persons accepted for insurance purposes might be applied to patients in clinical medicine. Certainly such assessments, if they could be made, would be very desirable. For example, a neurosurgeon remarked that, before operating on a man for brain tumor, he wished he could tell how old the man really was.

Whether an assessment of biologic age would be useful in predicting longevity or premature physical and mental disability could only be answered by long-term studies.

Summary

1. Assessment of physiologic age in an individual cannot be made on the functional capacity of any one physiologic system, but only by combining the various physiologic functions that show change with age.

2. The usual methods of expressing age in terms of physiologic function do not enable one to combine the various functions to give a single index of physiologic age.

3. A method is presented for assessing physiologic age in an individual based on the examination of five physiologic functions in a sample of 38 men between the ages of 21 and 84 years. Age is expressed in terms of a combination of the five physiologic functions and the squares of those functions. The method is applicable when the chronologic ages are randomly selected and can be used with an unlimited number of physiologic, anatomic, and psychologic criteria, to give an assessment of *biologic* age.

4. The distribution of the deviations between the estimated physiologic ages and the chronologic ages of the 38 men are recorded. So far as could be shown, the equation was equally applicable at all age periods. The standard error of the estimated physiologic age was 7.35 years and the question is raised whether one would expect to reduce this variation with a larger sample and by testing many more features.

5. Random samples of life insurance policyholders may be more nearly represenative of a large section of the general population than samples from any other specific group. Stanards based on such a sample could be used in assessing applicants for life insurance and also might be applicable to patients in clinical medicine.

6. Predictions of premature physical and mental disability or longevity, based on assessment of biologic age, must await the test of time.

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References

1. Bernstein, F., and Bernstein, M.: Law of Physiologic Aging as Derived from Long Range Data on Refraction of the Human Eye. *Arch. Opth., 34:* 378-388, 1945.
2. Birren, J. E., Bick, M. W., and Fox, C.: Age Changes in the Light Threshold of the Dark Adapted Eye. *J. Gerontol., 3:* 267-271, 1948.
3. Bunch, C. C.: Age Variations in Auditory Acuity. *Arch. Otolaryng., 9:* 625-636, 1929.
4. Bunch, C. C.: Further Observations on Age Variations in Auditory Acuity. *Arch. Otolaryng., 13:* 170-180, 1931.
5. Chieffi, M., and Kirk, E.: Vitamin Studies in Middle-Aged and Old Individuals. II. Correlation Between Vitamin A Plasma Content and Certain Clinical and Laboratory Findings. *J. Nutrition, 37:* 67-79, 1949.
6. Cullumbine, H., Bibile, S. W., Wikramanayake, T. W., and Watson, R. S.: Influence of Age, Sex, Physique and Muscular Development on Physical Fitness. *J. Applied Physiol., 2:* 488-511, 1950.
7. Donders, F. C.: *Accommodation and Refraction of the Eye.* New Sydenham Soc., London, 1864.
8. Fisher, R. A.: *Statistical Methods for Research Workers,* 8th. Ed., Oliver and Boyd, Ltd., Edinburgh and London, 1943.
9. Mainland, D.: Statistical Methods in Medical Research. I. Qualitative Statistics. *Canad. J. Research, E, 26:* 1-166, 1948.
10. Miller, I.: Blood Pressure Studies in the Aged. *New York State J. Med., 41:* 1631-1635, 1941.
11. Robertson, G. W., and Yudkin, J.: Effect of Age upon Dark Adaptation. *J. Physiol., 103:* 1-8, 1944.
12. Russek, H. I., Rath, M. M., Zohman, B. L., and Miller, I.: The Influence of Age on Blood Pressure. A Study of 5,331 White, Male Subjects. *Am. Heart J., 32:* 468-479, 1946.
13. Snedecor, G. W.: *Statistical Methods,* 4th. Ed. The Collegiate Press, Inc., Ames, Iowa, 1948.
14. Stevens, W. L.: The Distribution of Groups in a Sequence of Alternatives. *Ann. Eugenics, 9:* 10-17, 1939.
15. Stuart, H. C., and Meredith, H. V.: Use of Body Measurements in the School Health Program. *Am. J. Pub. Health, 36:* 1365-1386, 1946.
16. Ufland, J. M.: Einfluss des Lebensalters, Geschlechts, der Konstitution und des Berufs auf die Kraft verschiedener Muskelgruppen. I. Mitteilung: Über den Einfluss des Lebensalters auf die Muskelkraft. *Arbeitsphysiol., 6:* 653-663, 1933.

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Studies in Experimental Atherosclerosis

II. Biochemical Effect of Intravascular Injection of Cholesterol Sols Into Animals

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For various reasons, cholesterol suspensions were injected into experimental animals subcutaneously (8, 10, 15, 26, 28), intraperitoneally (9), or into various parts of the eye (23). Of the scientists who introduced cholesterol into blood circulation, two injected into the portal vein (6, 27), while all the others used one of the peripheral veins (1-7, 11-14, 16-22, 24, 25). Rabbits, rats, cats, dogs, and even human beings were injected with cholesterol sols or with preparations containing cholesterol. Curiously, not all of the investigators recorded blood chemical changes after intravascular injections. We find it advisable to review all reports for nowhere can a survey of these experiments be found in the literature.

Historical Data

The majority of scientists reported reversible blood cholesterol rise after intravascular injection of cholesterol sols. Such observation was made by Deicke (7), regardless of whether a single or multiple intravenous injections of cholesterol in olive oil or of a hydrosol were made into rabbits. Kaufer (14) recorded a temporary rise of the blood cholesterol of rabbits immediately following intravenous injection of a 3 to 5 per cent cholesterol hydrosol.

Injection of a similar preparation into the jugular vein of cats resulted, according to Dahmlos (6) and to Stuber (25), in a lipemia which lasted six hours. Kendall (16) and Bevans, Abell, and Kendall (2, 3), who injected rabbits intravenously with 2.5 per cent cholesterol sol stabilized with sodium stearate, demonstrated a sharp increase in blood cholesterol ten minutes after injection, a gradual decrease within six hours, a second but less marked rise after twenty-four hours, and a return to the initial blood level within seventy-two hours after injection. The initial peak was 250 to 300 mg. above the base level, while after six hours the cholesterol value was 100 to 150 mg. above the norm. During the period of fall of the curve for free cholesterol there was a moderate rise in cholesterol esters.

Similar observations were made by Byers and Friedman (1), who injected rats intravenously with cholesterol in a mixture of lauric acid and lactic acid in a dose of 20 mg. per 100 Gm. body weight. In their series, the level of free cholesterol rose sharply within fifteen minutes and slowly returned to normal within thirty-six hours after injection.

Chamberlain (5) found that three to forty-eight hours after intravenous injection of 150 to 250 mg. of cholesterol-oleic acid suspension the blood cholesterol levels of rabbits averaged 50 per cent more than prior to injection. Nomura (19) observed a rapid rise and a slow fall of blood cholesterol in man upon intravenous injection of "yanol," a mixture of butter, cod liver oil, and lecithin. Hirsch (11) could double blood cholesterol levels of rabbits by weekly intravenous administration over a period of months of human fat with added cholesterol, or of human fat with oleic acid, or of a fat mixture.

Horlick, Feldman, and Katz (12), who infused hypercholesteremic blood plasma from one series of chickens to another, plotted curves which showed a fast rise of blood cholesterol within fifteen minutes and a slow return to the original level within twenty-four hours. The speed at which cholesterol disappeared from the blood stream was directly proportional to the height of the cholesterol value. The ratio between free and esterified cholesterol

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remained normal throughout their experiment.

In sharp contrast with such data seem the reports of Cashin and Moravek (4) on a 20 to 60 per cent drop of the blood cholesterol level of cats one hour after intravenous injection of a cholesterol-lecithin mixture. In variation with the majority of reports was also the communication of Remesov (21), who produced a fourteen day lasting hypercholesteremia in rabbits by intravenous injection of 5 mg. of dialyzed cholesterol suspension per Kg. body weight and in dogs by injection of 50 mg. per Kg. body weight for ten days. Leites (17, 18) and Derman and Leites (8) injected dogs intravenously with a modified Porges-Neubauer (20) cholesterol suspension but failed to report changes in the blood cholesterol level. A similar suspension injected repeatedly to rabbits by Dewey (9) did not influence the blood cholesterol.

Leites (17, 18) concluded that cholesterol was absorbed in the lungs and spleen where a split of lipoids took place in the course of his experiments. Remesov and Tavaststyerna (22) ascribed lasting hypercholesteremia to inhibition of lipase by cholesterol. They saw in the cholesterol—cholesterol ester ratio a real buffer system which is held in constant equilibrium and is destined to protect the organism against saturation with free cholesterol. The two protective mechanisms were thought to be esterification and rapid excretion of free cholesterol. Deicke (7) attempted to explain the differences in the findings of various investigators by the variable individual reactivity of experimental animals.

Experimental

The contradictory reports concerning blood cholesterol levels after intravenous injection of colloidal cholesterol warranted renewed investigation of the problem. As our experiments were primarily designed to study anatomic alterations induced by intravascular administration of cholesterol sols, the amount of cholesterol introduced by us into rabbits was mostly too small to influence the blood cholesterol level. This resulted in elimination of a number of animals from this report.

The average weight of 50 rabbits of the same breed whose blood was analyzed before and after intravascular injection of cholesterol sols was 2.5 Kg. The average total amount of cholesterol injected was 100 mg., that is, 40 mg. per Kg. of body weight. There were but moderate deviations from the average values in the series of rabbits selected for this analysis.

Series No. 1. A single intravenous injection was given to 32 rabbits. In blood samples withdrawn immediately upon completion of the injection, within thirty seconds, the cholesterol value was always 20 per cent below the initial level. Five minutes after injection the value equaled that ascertained before injection. After fifteen minutes, the blood cholesterol level was 8.5 per cent above the base value. It was 20 per cent above the initial value in samples secured twenty and sixty minutes after injection.

Series No. 2. Ten rabbits were injected twice. The amount of cholesterol administered was divided into two equal doses. Blood was drawn after the second injection only. At

first, the cholesterol curve resembled that plotted after a single injection. The cholesterol value was 20 per cent below the base line five minutes after the injection and still 13.5 per cent below the norm fifteen minutes after injection. The initial value was reached within twenty to thirty minutes. From now on, the curve differed from that after single injection. The blood cholesterol value climbed to 20 per cent above the norm within forty-five minutes, to 40 per cent in sixty minutes, and it was 50 per cent above the initial value six hours after the injection. The results were the same whether the second injection was given one, twenty-four, forty-eight, or seventy-two hours after the first one.

Series No. 3. Eight animals were injected three to four times. The results were quite different from those observed after one or two administrations of cholesterol. Blood taken seven minutes after the third injection contained on the average 40 per cent more cholesterol than before the injection. Blood taken fifteen minutes after the fourth injection had, in 4 rabbits, on the average 80 per cent more cholesterol than at the onset of the experiment. Seven days after the third or fourth injection of cholesterol sols, the blood level was twice as high as prior to the injections. The total increase of blood cholesterol equaled up to 75 per cent of the total amount injected in three to four doses. In one-half of these rabbits, injections were given twenty-four hours apart, and in the other half, five to nine days elapsed between the injections.

All rabbits were injected with cholesterol sols for which partly deproteinized rabbit serum was used as stablizer (see article 1 of this series, Journal of Gerontology, *6:* 1-6, 1951). The results of blood chemical analyses were essentially the same whether a suspension with "coarse" particles measuring 0.2 to 0.4 μ or a "fine" suspension with micels measuring 0.02 to 0.04 μ were injected. In each group of animals results were uniform. All determinations were made by the Sperry-Schoenheimer method.

Analysis

The biochemical effect of the introduction of cholesterol into the blood stream attracted much attention. Evaluation of results of various investigators is difficult because of the many variants entailed in their experiments. There are differences in the cholesterol sols and other colloidal preparations used for injection. There are variations in doses, in the intervals between injections, in the number of injection, in the duration of the experiments, and finally, in the animal species studied.

By comparison with experiments of others, the quantity of cholesterol we introduced into the circulation of rabbits was small. The average dose we used was 40 mg. per Kg. body weight. A maximum of four injections was given to a rabbit of our series. The experiment did not extend over two weeks. Other investigators injected over months or beyond one year; the number of injections was commonly very great and the total dose of cholesterol large.

Our observations confirmed many of the previous claims. Intravenous injection of cholesterol sol was always followed by an immediate drop of the blood cholesterol level, suggesting absorption of the cholesterol by tissues, possibly the vessel wall. This phase lasted in our experiments from five to fifteen minutes. After this time, cholesterol reappeared in the blood stream and this seemed indicative of resorption of cholesterol deposits from vessels and transportation of the cholesterol to a secondary depot, presumably the liver.

The maximum cholesterol level obtained was proportional to the number of injections rather than to the total amount of cholesterol introduced. This would indicate a cummulative effect. In not a single instance could the total amount of cholesterol administered be recovered. The difference between the amount injected and the amount recovered was 25 per cent or more, certainly beyond the limits of errors inherent to the chemical method employed. It can be assumed that a portion of

the cholesterol injected is retained in the viscera of the experimental animals.

Summary

1. The literature relative to the biochemical effect of intravascular injection of cholesterol into experimental animals has been reviewed.

2. Observations made on 50 rabbits injected intravascularly with cholesterol sols are reported.

3. Intravenous injection of cholesterol sols into rabbits is followed by an initial drop of the blood cholesterol level and a subsequent gradual rise of the blood cholesterol.

4. An attempt is made to explain the various phases of the blood cholesterol curve plotted after intravenous injection of colloidal cholesterol as well as to explain the failure to recover the total amount of material injected.

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References

1. Byers, S. O., and Friedman, M.: Hypercholesteremia in the Rat after Intravenous Administration of Cholesterol. *J. Biol. Chem., 177:* 841-846, 1949.
2. Bevans, M., Abell, L. L., and Kendall, F. E.: Production of Intimal Atherosclerosis by Intravenous Injection of Colloidal Cholesterol into Rabbits. *Federation Proc., 7:* 269, 1948.
3. Bevans, M., Kendall, F. E., and Abell, L. L.: Development of Atheromatous Plaques Following Production of Intimal Atherosclerosis by Intravenous Injection of Colloidal Cholesterol into Rabbits. *Am. Heart J., 36:* 473, 1948.
4. Cashin, M. F., and Moravek, V.: The Physiological Action of Cholesterol. *Am. J. Physiol., 82:* 294-298, 1927.
5. Chamberlain, N.: The Cholesterol Content of Normal Tissues and the Effect of Intravenous Injection of Cholesterol Thereon, *J. Physiol., 66:* 249-261, 1928.
6. Dahmlos, J.: Permeabilitätsstudien. IV. Mit. Leber- und Lipoidfunktion. *Biochem. Ztschr., 242:* 88-120, 1931.
7. Deicke, O.: Beobachtungen an Kaninchen mit künstlicher Cholesterinzufuhr. *Krkhtsforsch., 3:* 399-418, 1926.
8. Derman, G. L., and Leites, S.: Experimentell-morphologische Studien über die Rolle der Lungen, Leber und Milz im Fett- und Lipoidstoffwechsel. *Virchows Arch. f. path. Anat., 268:* 440-455, 1928.
9. Dewey, K.: Experimental Hypercholesterolemia. *Arch. Int. Med., 17:* 757-785, 1916.
10. Garschin, W. G.: Ueber einige Bedingungen für die Ablagerung doppeltlichtbrechender Lipoide in den Zellen, *Centralbl. f. allg. Path. u. path. Anat., 35:* 75, 1924-25.
11. Hirsch, E. F.: Experimental Tissue Lesions with Mixtures of Human Fat, Soaps and Cholesterol. *Arch. Path., 25:* 35-39, 1938.
12. Horlick, L., Feldman, M., Jr., and Katz, L. N.: Disappearance of Cholesterol Following Its Intravenous Injection in Physiologically Emulsified Form. *Proc. Soc. Exper. Biol. & Med., 68:* 243-245, 1948.
13. Kaeser, E.: Studien über Cholesterin und seine Ester. *Biochem. Ztsch., 154:* 321-327, 1924.
14. Kaufer, L.: Experimentelle Untersuchungen mit intravenöser Cholesterinzufuhr. *Ztschr. f. d. ges. exper. Med., 62:* 571-584, 1928.
15. Kawamura, R.: *Die Cholesterinesterverfettung* (Cholesterinsteatose), J. Fischer, Jena, 1911.
16. Kendall, F. E.: *Degenerative Lesions of Metabolism.* Seminar Program, Oct. 1947, sponsored by Metabolism and Endocrinology Study Section. N. I. H., U.S.P.H.S.
17. Leites, S.: Studien über Fett- und Lipoidstoffwechsel. VI. Über die Rolle der Lungen im Fett- und Lipoidstoffwechsel. *Biochem. Ztschr. 190:* 286-303, 1927.
18. Leites, S.: Studien über Fett- und Lipoidstoffwechsel. Über Fettabbau im Tierischen Organismus bei Fettbelastung. *Biochem. Ztschr., 197:* 357-362, 1928.
19. Nomura, T.: Experimentelle Studien über intravenöse Fettinfusion unter besonderer Berücksichtigung parenteraler Ernährung. I. Schwankung des Fettgehaltes im Blute nach Fettinfusion. *Tohoku J. Exper. Med., 12:* 247-253, 1929.
20. Porges, O., and Neubauer, E.: Physikalisch-chemische Untersuchungen über das Lecithin und Cholesterin. *Biochem. Ztschr., 7:* 152-177, 1908.
21. Remesov, I.: Physikalisch-chemische Untersuchungen über die Veränderungen des Blutes bei der experimentellen Cholesterin-Atherosklerose. *Pflüger's Arch. f. d. ges. Physiol., 221:* 534-548, 1929.
22. Remesov, I., and Tavaststyerna, N.: Experimentell-chemische Studien über den Lipoidstoffwechsel. I. Über die Hypercholesterinämie bei Omnivoren und Herbivoren, hervorgerufen durch parenterale Belastung mit kolloidem Cholesterin und Lecithin. *Ztsch. f. d. ges. exper. Med., 76:* 419-462, 1931.

23. Rohrschneider, W.: Über die Bildung intracellulärer anisotroper Tröpfchen nach örtlicher Einspritzung von Cholesterin in die Cornea und Vorderkammer des Kaninchen Auges. *Virchows Arch. f. path. Anat., 256:* 150-157, 1925.
24. Stern, R.: Über die klinische Bedeutung des Cholesterins in der Galle und im Blutserum. *Arch. f. exper. Path. u. Pharmakol., 112:* 129-175, 1926.
25. Stuber, B.: Über Blutlipoide und Phagocytose. I. *Biochem. Ztschr., 51:* 211-223, 1913.
26. Wacker, L., and Hueck, W.: Chemische und morphologische Untersuchungen über die Bedeutung des Cholesterins im Organismus. *Arch. f. exper. Path. u. Pharmakol., 74:* 416-441, 1913.
27. Wohlwill: Experimentelles zur Pfortadersklerose. *Verhandlg. d. deutsch. path. Gesellsch., 22:* 235 237, 1927.
28. Zinserling, W.: Über die Anfangsstadien der experimentellen Cholesterinverfettung. *Beitr. z. path. Anat. u. z. allg. Path., 71:* 292-315, 1923.

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The Excretion of Pantothenic Acid in the Urine in Young and Old Individuals

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Since the signs and symptoms of pantothenic acid deficiency in human individuals are not known with certainty methods other than the clinical examination must be used to demonstrate a possible deficit of this vitamin. In the past several attempts have been made to disclose pantothenic acid deficiency through measurement of the spontaneous urinary excretion of pantothenic acid or the excretion following pantothenic acid administration. Several of these studies cannot, however, be considered conclusive since the analytic methods employed have not been sufficiently specific.

The spontaneous excretion of pantothenic acid was investigated in 1941 by Pelczar and Porter (4) by a study of 9 normal individuals. The daily pantothenic acid excretion averaged 3.88 mg. (1.46 to 6.79 mg.); the pantothenic acid determinations were made microbiologically, using Proteus morganii. In the same year, Strong, Feeney, and Earle (6), using Lactobacillus casei for the assay, reported an excretion of 2 to 6 micrograms per milliliter of urine, whereas Skeggs and Wright (5), employing Lactobacillus arabinosus, observed an excretion of 8.7 micrograms per milliliter. Since the diuresis is not given the results in these latter publications are not directly comparable with those of Pelczar and Porter (4).

An important feature in the estimation of the urinary content of pantothenic acid is the fact that bacterial contamination with pantothenic acid producing bacteria may result in analytic values several times higher than the real values. The avoidance of bacterial infection during the analysis is therefore of the greatest importance. This precaution was observed by Pelczar and Porter (4) but is not mentioned in the publications by Strong, Feeney, and Earle (6) or Skeggs and Wright (5).

Investigations on the excretion of pantothenic acid after pantothenic acid administration have been performed by Pearson (3) and by Burlet (1). In Pearson's studies 1000 mg. of calcium pantothenate were ingested by 3 normal adults and the pantothenic acid excretion in the urine measured over a twenty-six hour period following the administration. The results showed an excretion of only 7.8, 11.7, and 6.8 per cent of the ingested pantothenic acid. In Burlet's experiments 250 mg. of calcium pantothenate was given by mouth to 2 normal individuals. This ingestion resulted in an excretion of 32 and 56 mg. of the vitamin; the spontaneous pantothenic acid excretion in the 2 subjects was 2 mg. and 7 mg. respectively. After ingestion of 250 mg. of panthenol, the excretions were 65 and 105 mg.

The present study was undertaken with the purpose of investigating the spontaneous pantothenic acid excretion and the pantothenic acid excretion following injection of pantothenic acid in a larger group of individuals of various ages.

Technique

For pantothenic acid determination in the urine the microbiologic compensation method of Nielsen, Hartelius, and Johansen (2) was employed, using Streptobacterium plantarum. This method permits the determination of pantothenate with an accuracy of 20 per cent. The urine was collected quantitatively in flasks containing 0.5 to 5 ml. of a 10 per cent thymol solution, giving a final thymol concentration in the urine sample of 1:2000. This concentration was found to be sufficient to prevent bacterial growth. For analysis of the pantothenic acid content a 100 ml. aliquot was used. If the analysis could not be undertaken immediately the urine sample was heated to boiling

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(100 C.) for five minutes and was afterwards stored in the refrigerator. The microbiologic analyses were performed on urine dilutions of 1:50 to 1:500.

Before the test load dose of pantothenic acid was decided upon, a special investigation was made of the spontaneous pantothenic acid excretion during the course of the day and night and also of the pantothenic acid excretion in successive urine samples collected quantitatively for twenty-four hours following the intramuscular injection of 25 mg. of panthenol.

The results of such investigations are presented in table 1, which shows that the spontaneous excretion is higher during the day than during the night. The excretion after pantothenic acid injection is usually highest during the first four hours after the administration of pantothenic acid; the excess urinary excretion is often still noticeable as late as sixteen hours after the beginning of the tolerance test. The use of a twenty-four hour urine collection period in pantothenic acid tolerance tests therefore appeared to be suitable.

Experimental

Investigations on the twenty-four hour spontaneous excretion of pantothenic acid and the excretion following intramuscular injection of 25 mg. of panthenol were made in 17 children between 2 and 14 years of age, in 56 adults (31 men, 25 women) aged 15 to 45 years, and in 23 older individuals (11 men and 12 women) over 50 years (51 to 82 years).

All the older individuals were grey-haired but none displayed signs of avitaminosis. The selection of grey-haired subjects for this more advanced age group was made purposely since on the basis of animal experiments it might be expected that evidence of pantothenic acid deficiency would more likely be found in this group than in individuals with normal pigmentation of the hair. The results of both the spontaneous pantothenic acid excretion and the excretion observed in the tolerance test are given in table 2.

The findings show approximately the same spontaneous pantothenic acid excretion in the children and the younger adults. Following panthenol administration, however, a slightly higher excretion of pantothenic acid was noted in the children than in the adults, an observation which is probably explainable on the basis of the smaller body size of the children.

As will further be seen from table 2, the daily spontaneous pantothenic acid excretion in the advanced age group was 2.3 ± 0.6 mg. as compared with 2.7 ± 0.7 mg. in the younger adults. Following the tolerance test the twenty-four hour pantothenic acid output was 6.6 ± 1.1 mg. in the older subjects as contrasted to 7.1 ± 0.7 mg. in the younger group. The difference between these sets of values is probably, but not definitely, significant.

Table 1. The Mean Spontaneous Pantothenic Acid Excretion and the Excretion Following Parenteral Administration of 25 mg. of Panthenol During Various Hours of the Day in 8 Normal Individuals.

	8 A. M. to 12 Noon Mg.	12 Noon to 4 P. M. Mg.	4 P. M. to 8 P. M. Mg.	8 P. M. to 12 Midnight Mg.	12 Midnight to 8 A. M. Mg.
Spontaneous Excretion	0.5	0.8	0.8	0.5	0.5
After Panthenol Administration	3.1	2.0	1.2	0.8	0.4

TABLE 2. THE 24 HOUR EXCRETION OF PANTOTHENIC ACID IN THE URINE BEFORE AND AFTER INTRAMUSCULAR ADMINISTRATION OF 25 MG. OF PANTHENOL

Age in Years	No. of Individuals	Pantothenic Acid Excretion in Mg.					
		Spontaneous			After Panthenol Injection		
		Mean	s. d.	Range	Mean	s. d.	Range
2—14	17	2.5	0.7	1.8—4.5	7.2	1.1	6.0—9.6
16—45	56	2.7	0.6	1.2—4.4	7.1	0.7	4.7—8.8
51—82	23	2.3	0.6	1.0—3.6	6.6	1.1	4.4—9.1

As elderly persons usually are not so physically active as younger individuals, the ingestion of food will also as a rule decrease with age. Consequently a reduced spontaneous excretion of pantothenic acid must be expected with advancing years. The observed reduced spontaneous excretion actually observed with age is therefore most probably explainable on the basis of a reduced food intake and does not warrant the conclusion that greyness of the hair in the aged is due to pantothenic acid deficiency.

If the greyness were associated with a deficit of pantothenic acid, the spontaneous excretion in the elderly as compared with the younger subjects would have been expected to be much lower than the decreases observed in this study. But in particular one would have expected a considerable difference in excretion between the younger and the older groups following the parenteral administration of 25 mg. of panthenol, indicative of a latent deficiency, and such great difference was not found in the present study.

SUMMARY

The pantothenic acid excretion in the urine was determined quantitatively in a large group of young, middle-aged, and older individuals, using the microbiologic assay method of Nielsen, Hartelius, and Johansen. All the older individuals included in this study were grey-haired. Studies were made both of the spontaneous twenty-four hour excretion and of the excretion following intramuscular injection of 25 mg. of panthenol.

The results showed a moderately lower excretion in the elderly subjects, both under normal conditions and following parenteral pantothenic acid administration. The lower excretion appears to be due to a decreased food intake and the findings do not support the contention that a pantothenic acid deficiency is found in old age, nor the assumption that achromotrichia is conditioned by such deficiency.

REFERENCES

1. Burlet, E.: Die biologische Umwandlung von Panthenol (γ-Oxypropylamid der 2. 4-Dioxy-3. 3-dimethylbuttersäure) in Pantothensäure. *Ztschr. f. Vitaminforsch, 14:* 318-331, 1944.
2. Nielsen, N., Hartelius, V., and Johansen, G.: Bestimmungen von Pantothensäure und β-Alanin in Tierischen und Pflanzlichen Objekten mit einer neuen Methode. *Compt. rend. d. trav. du lab. Carlsberg, serie physiol., 24:* 97-116, 1945.
3. Pearson, P. B.: Studies on the Metabolism of Pantothenic Acid in Man and Rabbits. *Am. J. Physiol, 135:* 69-76, 1941.
4. Pelczar, M. J., Jr., and Porter, J. R.: Determination of Pantothenic Acid in Normal Blood and Urine by Microbiological Technic. *Proc. Soc. Exper. Biol. & Med., 47:* 3-7, 1941.
5. Skeggs, H. R., and Wright, L. D.: The Use of Lactobacillus Arabinosus in the Microbiological Determination of Pantothenic Acid. *J. Biol. Chem., 156:* 21-26, 1944.
6. Strong, F. M., Feeney, R. E., and Earle, A.: Microbiological Assay for Pantothenic Acid. *Indust. & Engin. Chem. (Analyt. Ed.), 13:* 566-570, 1941.

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Plasma Uric Acid in Aged and Young Persons

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USING A NEW SPECIFIC METHOD FOR URIC ACID DETERMINATION DR. PRÆTORIUS STUDIED THE PLASMA URIC ACID CONCENTRATION IN 170 YOUNG AND OLD INDIVIDUALS. THE MEAN URIC ACID CONTENT OF PLASMA WAS FOUND TO BE LOWER IN THE WOMEN THAN IN THE MEN AND SHOWED A TENDENCY TO INCREASE WITH AGE IN THE WOMEN.

THE available data on the concentration of uric acid in the plasma or serum of human individuals are based on analyses performed with colorimetric or titrimetric methods. The specificity and accuracy of these methods are however, not great. Thus, a loss of uric acid frequently takes place during the protein precipitation employed in the preparation of protein-free filtrates, whereas, on the other hand, substances other than uric acid in the filtrates may contribute to the color development. This subject has recently been reviewed in detail (2).

The recent introduction by Kalckar (1) of a specific method for uric acid determination constituted a significant advance in the analysis of this compound and made it desirable to repeat previous studies with the purpose of establishing the normal plasma uric acid concentration at various ages.

The method of Kalckar is based on differential enzymatic spectrophotometry. The absorption of ultraviolet light (wave length 292.5 $\mu\mu$) by uric acid is measured before the addition of uricase and again after the uric acid has been split by the enzyme. The decrease in optical density observed after the action of uricase is directly proportional to the amount of uric acid in the samply. Because of the very high molar extinction of uric acid in the ultraviolet light, which between the wave lengths 290 and 295 $\mu\mu$ has a maximum of 12,000, this method offers a much higher sensitivity than other enzymatic methods.

The application of the method to plasma and other biologic fluids has been described in detail (2). For the convenience of the reader a brief outline of the analytic technique will be given here.

METHODS

By means of a Carlsberg constriction pipette 268.5 cu. mm. of stabilized plasma were transferred to a 10 ml. volumetric flash containing 1 ml. of 2/3 molar glycine buffer (pH 9.1 to 9.4) and the volume made up to 10 ml. with distilled water. Three ml. of the diluted sample were measured into a silica cell and 2.5 ml. into a reference cell of a Beckman spectrophotometer DU. By the addition of about 0.5 ml. of distilled water to the reference cell an extinction difference of 0.200 to 0.400 at 292.5 $\mu\mu$ between the two cells was easily obtained.

After a constant initial reading had been obtained 10 cu. mm. of a highly purified uricase suspension were added to the contents of the measuring silica cell and the extinction at 292.5 $\mu\mu$ was read at 10 to 15 second intervals for a period of one to two minutes, the extinction values and the times in seconds as read on a stop watch being noted. From these data an extrapolation of the extinction to zero time was made possible.

After the initial reaction period readings of the extinction were made at intervals of 10 to 15 minutes until the reading remained constant. The difference between the extrapolated extinction value and the final constant extinction reading multiplied by 50 represents the plasma uric acid in milligrams per 100 ml.

The study comprises analyses of the plasma uric acid concentration in 130 individuals between the ages of 41 and 102 years (61 men and 69 women) and in 40 younger persons (24 men and 16 women) between 20 and 39

TABLE 1. PLASMA URIC ACID CONCENTRATION IN 85 MEN OF VARIOUS AGES

Age	Plasma Uric Acid Mg. %	Age	Plasma Uric Acid Mg. %
21	5.65	66	5.30
24	5.25	66	4.45
24	4.75	66	5.80
24	5.00	66	5.15
24	4.80	67	4.90
24	4.00	67	5.40
24	5.65	67	5.15
25	4.25	67	3.35
25	5.00	68	4.90
25	6.55	69	5.15
26	3.35	69	4.60
27	6.00	69	5.40
27	4.30	70	5.80
27	5.05	70	6.65
28	3.55	70	6.65
28	4.45	71	3.90
28	4.65	71	5.70
28	5.80	71	5.45
29	9.70	71	3.80
29	4.15	71	4.10
32	5.20	72	5.45
32	3.50	72	3.15
34	4.85	73	4.00
37	7.40	74	4.25
39	3.80	74	9.00
40	5.45	75	7.10
41	8.45	75	4.90
43	3.80	75	5.00
43	3.75	75	3.90
44	6.65	76	2.50
45	6.75	77	8.40
49	2.85	77	3.25
50	4.35	78	6.35
58	3.95	80	7.30
60	4.80	80	4.45
61	4.30	82	5.90
62	6.10	82	3.85
64	3.40	83	2.60
64	3.50	83	7.25
65	4.50	83	3.30
65	3.90	84	6.40
65	3.90	87	3.70

years of age. The majority of the older subjects were inmates or patients in the St. Louis City Infirmary and City Infirmary Hospital, whereas the greater part of the younger individuals were private volunteers. None of the patients suffered from gout or any other disease characterized by increased plasma uric acid, and none of the old persons had an NPN value higher than 50 mg. per 100 ml. of plasma. All the younger persons were apparently without any disease.

The blood samples were drawn from the cubital vein at 8:00 a. m., centrifuged one or

TABLE 2. PLASMA URIC ACID CONCENTRATION IN 97 WOMEN OF VARIOUS AGES

Age	Plasma Uric Acid Mg. %	Age	Plasma Uric Acid Mg. %
20	3.75	72	3.75
21	3.60	73	3.75
22	2.80	74	4.45
23	4.00	74	3.85
24	4.35	75	4.05
24	3.25	75	4.40
29	2.90	75	2.70
29	2.20	75	3.70
33	3.35	75	3.30
33	4.65	76	2.40
35	3.65	76	4.80
36	3.10	76	5.70
36	3.70	76	4.40
36	3.55	76	2.55
38	3.25	76	2.95
38	3.85	76	3.20
42	2.60	77	3.30
49	6.15	77	4.00
50	3.25	77	5.30
52	2.20	77	3.35
54	4.40	77	3.65
54	2.50	77	4.45
54	4.60	77	3.15
57	4.10	77	4.60
58	3.65	78	3.55
58	3.05	78	5.20
59	5.30	78	4.75
61	5.45	78	4.50
61	5.25	79	5.45
61	3.40	79	3.65
61	3.40	80	2.95
62	6.10	80	3.35
62	2.60	80	3.35
62	3.40	80	5.05
65	4.30	81	4.55
66	5.70	81	3.15
66	3.10	82	3.65
67	3.05	83	5.00
67	3.10	83	2.60
67	3.10	84	4.05
67	3.70	84	3.90
69	5.05	84	3.85
69	2.90	85	3.35
69	3.65	85	4.30
69	4.20	86	2.45
70	2.50	87	5.70
72	4.05	92	4.10
72	5.35	102	3.60

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two hours later, and the uric acid content of the plasma determined immediately.

Results

The results obtained in the various age groups are presented in tables 1 and 2, which show a mean value of plasma uric acid for young men and young women of 5.1 and 3.5 mg. per cent, respectively. For the older age group the corresponding figures are 5.0 and 4.0 mg. per cent. Statistical calculation of the data shows that the difference in the average plasma uric acid values between young men and young women and between old men and old women are significant, the "t" values being 5.35 and 3.6, respectively. This sex difference in plasma uric acid concentration has also been noted by previous investigators. If the younger age groups are compared with the older age groups it will further be noted that there exists a statistically significant difference between the younger and the older women, the "t" value of this difference being calculated to 2.6. On the other hand, the figures do not reveal any definite change with age in the plasma uric acid concentration in the men.

Summary

Results are reported of plasma uric acid determinations of 170 individuals. The uric acid determinations were performed by enzymatic differential spectrophotometry. The findings showed a significantly lower plasma uric acid value in the women than in the men and further revealed a tendency for the uric acid content to increase with age in the women but not in the men.

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References

1. Kalckar, H. M.: Differential Spectrophotometry of Purine Compounds by Means of Specific Enzymes. *J. Biol. Chem., 167:* 429-443, 1947.
2. Prætorius, E.: An Enzymatic Method for the Determination of Uric Acid by Ultraviolet Spectrophotometry. *Scand. J. Clin. Lab. Invest., 1:* 222-230, 1949.

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The Social Roles of Old People

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THE purpose of this study was two-fold; first, to identify the activities or social roles of older people in an average community, and second, to find out how these social roles were related to the personal adjustment of older people. In a general way it was thought that the active aged were also well adjusted. This study was aimed at obtaining objective evidence for this hypothesis.

METHODS

Selection of the community.—The mid-western town selected for this study had a population of over 6,000 with about 10 per cent of the people over 65 years old. It was supported by several small industries and was the county seat and main shopping center for a large rural area. Various census criteria were used to select it as typical for this region.

Selection of the subjects.—Selection of the 100 subjects in this study was made by the proportional sampling method. Their social status position was established by Warner's Index of Status Characteristics and they represented the upper, upper middle, lower middle, upper lower, and lower lower classes (4). Subjects were then selected from these five status groups according to age, sex (55 women and 45 men), and marital status to retain the proper percentage proportions of the larger population of aged in that community.

Collection of the data.—The subjects were interviewed by use of the focused interview described by Merton and Kendall (3). Factual data were recorded on the schedule *Your Activities and Attitudes* (1). Expression of feelings was stimulated by nondirective methods. Information obtained was substantiated by reliable acquaintances, and court house records and newspaper items furnished additional data.

Measurement of role-activities and personal adjustment.—Two instruments were used to evaluate role-activities and personal adjustment:

1. A scale was devised to measure the activities of the aged in selected role-areas. The term role-area was used as an over-all designation of a more general area in which activities were possible. Those role-areas selected for this study were:

   A. Parental (including those of the parents, grandparents, and great-grandparents)
   B. Home responsibilities
   C. Kinship interaction
   D. Participation in clubs and organizations
   E. Church activities
   F. Civic and community activities

Ten role-activities were defined in each area. Rejection or nonparticipation received a low score, high activity a high score, and scores between the two extremes indicated the various stages of activity on a rising scale.

2. The Adjustment Rating Scale designed by Cavan (2) was used to rate the subject's general degree of personal adjustment in later maturity. It included a ten point scale in six areas:

   A. Personal, intimate association with family and friends
   B. Group associations and contacts with the world through reading and radio
   C. Individual activities and hobbies
   D. Feelings of emotional security in relation to friends, family, and religion
   E. Feelings of status and social recognition
   F. Happiness and contentment

Each subject was rated in every area by the interviewer and at least three judges. The composite formed the individual's score in that particular area.

The following report shows the larger patterns of role-activities as they emerge from the

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more detailed study. All statistical results reported utilized the ten-point scales.

Results

Parental and home centered role-activities.—Seventy-eight per cent of the sample were parents of living children. They had a total of 303 living children, an average of 3.88 children per parent. Seventy per cent of the sample population were grandparents, with 495 living grandchildren, or an average of 7.07 per person. Only 23 per cent were great-grandparents, with 116, or an overage of 5.04 great-grandchildren per person. The numbers included legally adopted children and those for whom the subjects had voluntarily accepted responsibility.

Parents showed five main divisions of responsibility for or interaction with the children (table 1).

Parents and children who were independent of each other were self-reliant even when they lived under the same roof. Social and affectional ties could be strong without turning to dependence. Aged parents had dependent children because of adoption, illness, marriage of an older man to a much younger woman, or ethnic culture patterns prolonging dependence. Mutual dependence was found when the parent was furnishing the home and the children took care of him or when the children had the home and the parent managed it. Parents were dependent mainly because of blindness or illness. Neglect by the children was found to stem from loss of contact in the earlier years; for example, one man released his son to his wife's relatives and lost track of him as the years went by but still reported himself as a father.

Product moment correlation coefficients were positive for all factors. The four parental correlations significant at the 1 per cent level were with home responsibility ($r = .64$), adjustment ($r = .53$), grandparent ($r = .50$), and social organizations ($r = .42$). Parental role-activities were related at the 5 per cent level only to kinship ($r = .23$). The last three correlations were possibly due to chance factors: great-grandparental roles ($r = .20$), civic ($r = .13$), and church ($r = .08$).

Parents who were independent of their children or had children dependent on them tended to be better adjusted than those who were dependent or had lost contact with the children. Independent parents took care of their own homes; they were moderately active in social organizations, attended church, voted in the elections, but took little responsibility in anything outside the home and family.

Grandparents varied their relationship as their grandchildren grew from infancy to adulthood. The role-activity patterns found are shown in table 2.

Grandparents took over the care of grandchildren while the parents worked, to relieve the parents for a few hours, or to have the

Table 1. Relation of Parents to Children (all numbers rounded to nearest percentage figure).

Relationship	Men (35)	Women (43)	Total (78)
Parents and children mutually independent	80	70	70
Parents with dependent children	6	9	6
Parents and children mutually dependent	3	12	9
Parents dependent on children	3	9	5
No contact with the children	8	0	4

TABLE 2. RELATION OF GRANDPARENTS TO GRANDCHILDREN (ALL NUMBERS ROUNDED TO NEAREST PERCENTAGE FIGURE).

Relationship	Men (30)	Women (40)	Total (70)
Full responsibility	0	0	0
Part time or occasional responsibility	20	27	24
Social participation only	73	70	72
Communication but no personal contact	0	0	0
No communication and no interest	7	3	4

pleasure of their company for overnight visits and other limited-time plans. Women took this responsibility for longer periods of time than men. Social participation without responsibility gave satisfaction with less expenditure of energy, and all of them were able to see their descendants at least occasionally if they kept up communication. Those who merely knew of the existence of grandchildren had broken relationships with their children (the parents of these descendants) years ago.

Grandparent role-activity ratings correlated at the 1 per cent level of significance with parent ratings ($r = .50$), home responsibility ($r = .46$), adjustment ($r = .45$), and civic activity ($r = .41$). Correlations at a 5 per cent level of significance were with social organizations ($r = .28$) and great-grandparent ($r = .50$). Correlations with kinship ($r = .19$), and church activity ($r = .19$) were possibly due to chance factors.

Table 3 shows the patterns of interaction of great-grandparents.

None of the great-grandparents lived in the same home with fourth generation members, but social interaction was obtained by individual visits, at family reunions and gatherings for special holiday celebrations. Greater distance separated fourth generation descendants for many of the aged but communication was carried on and pictures of the great-grandchildren frequently replaced those of the second and third generation for prominent display. Only the old people who lost track of their grandchildren had no interest in further decendants.

Active great-grandparents tended to be well adjusted as measured by the scale. The correlation coefficient with adjustment ($r = .68$) and with home responsibility ($r = .53$) showed significance at the 1 per cent level. Of lower significance (5 per cent) were the correlations with grandparent ratings ($r = .50$), church ($r = .45$), and kinship ($r = .44$). Social ($r = .33$), civic ($r = .31$), and parent ($r = .20$) correlations were possibly due to chance factors.

Family-minded aged who were in close contact with their descendants tended to be active as well as personally well adjusted. Compari-

TABLE 3. RELATION OF GREAT-GRANDPARENTS TO GREAT-GRANDCHILDREN (ALL NUMBERS ROUNDED TO NEAREST PERCENTAGE FIGURE).

Relationship	Men (7)	Women (16)	Total (23)
Full responsibility	0	0	0
Occasional or part time responsibility	0	6	4
Social participation only	57	57	57
Communication without personal contact	29	31	30
No interest and no communication about descendants	14	6	9

TABLE 4. MEAN ADJUSTMENT ON THE TEN POINT SCALE (SCALE VALUES RANGED FROM 0 TO 9).

Total sample population mean	5.000
Parent mean	5.115
Grandparent mean	5.157
Great-grandparent mean	5.043

son of the mean scores showed that old people who were parents were better adjusted than the average aged population.

Home responsibility patterns for combined role-activity scores showed the distribution for the entire sample as listed in table 5.

ship significant at the 5 per cent level was observed with social factors ($r = .22$) whereas the noted correlation with church activities ($r = .13$) was possibly due to chance factors.

The kinship or extended family group was a potential source of stimulation and interest

TABLE 5. DISTRIBUTION OF HOME RESPONSIBILITY PATTERNS FOR COMBINED ROLE-ACTIVITY SCORES (ALL NUMBERS ROUNDED TO NEAREST PERCENTAGE FIGURE).

Degree of Responsibility	Men (45)	Women (55)	Total (100)
Full responsibility for the home	13	20	17
Responsibility shared with spouse or others	65	63	64
No responsibility but helped a little	0	9	5
In an institution, helped some, cared for self	4	4	4
No home responsibility	18	4	10

Old people without responsibility were ill, lived in the homes for the aged and did not wish to work or could not do so, or they lived in a rooming house where they merely paid the rent.

Home responsibility ratings showed coefficients of correlation significant at the 1 per cent level with six factors; parent ($r = .64$), great-grandparent ($r = .53$), grandparent ($r = .46$), adjustment ($r = .42$), civic ($r = .34$), and kinship ($r = .28$). Relation-

to the old person. It included brothers and sisters, nephews and nieces, in-laws, cousins, and others who were considered relatives by the subjects. The fact that they lived near each other did not necessarily indicate interaction. One brother and sister in the sample did not even mention each other, but other subjects frequently mentioned cousins and relatives as far removed as grandnieces. The distribution of kinship role-activity rating are summarized in table 6.

TABLE 6. DISTRIBUTION OF KINSHIP ROLE-ACTIVITY RATINGS (ALL NUMBERS ROUNDED TO NEAREST PERCENTAGE FIGURE).

Relationship to Relatives	Men (45)	Women (55)	Total (100)
Frequent visits with relatives	29	42	36
Occasional contact with relatives	31	29	30
Correspondence but little contact	20	22	21
Little interest and no contact	20	2	10
No living relatives	0	5	3

Kinship ratings were found to correlate at the 1 per cent level of significance with four factors; adjustment ($r = .49$), civic ($r = .46$), social ($r = .33$), and home ($r = .28$). Correlation coefficients of less significance (5 per cent) with kinship were great-grandparent ($r = .44$) and parent ($r = .23$). Grandparent ($r = .19$), and church ($r = .14$), correlations were possibly due to chance factors.

Role-Activities Outside the Home.—Role-activities outside the family and home were centered in social clubs, the church, and the community.

The social groups of the town included clubs, lodges, parent-teacher associations and other groups with formal regulations, elected officers, stated purposes for existence, and compulsory dues. The aged showed a distribution of activity and interests in these social organizations as illustrated in table 7.

Social organization ratings were correlated at the 1 per cent level of significance with five factors; adjustment ($r = .52$), parent ($r = .42$), civic ($r = .37$), church ($r = .33$), and kinship ($r = .33$). Correlations of less significance (5 per cent) were found with grandparent ($r = .28$), and home ($r = .22$); correlation with great-grandparent ($r = .33$) was possibly being due to chance factors.

Church centered role-activities included participation in the organized church and devotions at home are shown in table 8.

Only the aged person with unusual ability and energy accepted a leadership position in the church organization. Women attended more faithfully than men and infrequent attendance was often blamed on the inability to negotiate the steps leading into the church. Radio listeners concentrating on religious services were either ill or had not affiliated with a church for the past twenty years or more.

Church activity was correlated at a significant level (1 per cent) with adjustment ($r = .31$) and social organizations ($r = .33$). Cor-

TABLE 7. DISTRIBUTION OF ACTIVITY AND INTERESTS IN SOCIAL GROUPS (ALL NUMBERS ROUNDED TO NEAREST PERCENTAGE FIGURE).

Degree of Participation	Men (45)	Women (55)	Total (100)
Active participant and held an office	2	13	8
Active participant, no responsibility	6	13	10
Frequent participant, no office	2	16	10
Occasional participant	16	13	14
No interest and no participation	74	45	58

Aged people were not officers of the large organizations, but were active in small, select groups. Women accepted responsibility and were active participants more than men.

TABLE 8. DISTRIBUTION OF CHURCH CENTERED ROLE-ACTIVITIES (ALL NUMBERS ROUNDED TO NEAREST PERCENTAGE FIGURE).

Relationship to Church	Men (45)	Women (55)	Total (100)
Faithful member and held church office	2	2	2
Church member, attended regularly	36	53	45
Church member, attended frequently	9	7	8
Devout, home service and radio-religion	7	9	8
Church member but seldom attended services	15	14	15
No church affiliation or attendance	31	15	22

relation of less significance (5 per cent) was found with great-grandparent ratings ($r = .45$). Grandparents ($r = .19$), kinship ($r = .14$), home ($r = .13$), civic ($r = .09$), and parent ($r = .08$) correlations were possibly due to chance factors.

Civic activity was possible for all but the very ill aged and credit was given for any interest in local and national affairs. Local political organizations sent cars to transport the infirm to the voting places, an exciting outing for many (table 9).

Civic ratings were correlated at the 1 per cent level of significance with five areas; kinship ($r = .46$), adjustment ($r = .44$), grandparent ($r = .41$), social ($r = .37$), and home ($r = .34$). Positive, but less significant relationships (possibly due to chance factors) were found with great-grandparent ratings ($r = .31$), parent ($r = .15$), and church activity ($r = .09$).

Personal Adjustment of the Aged.—The Cavan Scale for Personal Adjustment in later maturity was used to rate the adjustment of each subject (table 10).

Women had a diversified adjustment pattern and outranked men at both extremes—in very good adjustment and in serious maladjustment. Personal adjustment of all subjects was significantly related to all role-activities as indicated. High activity in any role-area was characteristic of some degree of adjustment,

TABLE 9. DISTRIBUTION OF CIVIC AND COMMUNITY ACTIVITIES (ALL NUMBERS ROUNDED TO NEAREST PERCENTAGE FIGURE).

Community Activities	Men (45)	Women (55)	Total (100)
Held a leading position in the community (mayor, alderman, etc.)	4	2	3
Attended open political meetings, read and discussed politics	18	7	12
Voted, but took no further part	69	56	62
Voted in local elections only	0	7	4
Did not participate in civic affairs	9	28	19

TABLE 10. ADJUSTMENT RATINGS OF EACH SUBJECT

Adjustment Ratings	Men (45)	Women (55)	Total (100)
Very well adjusted Well rounded social life, feeling of security, rapid adjustment to emotional disturbances	2	9	6
Moderately well adjusted Fairly well balanced social pattern without serious gaps, positive emotional patterns	36	31	33
Average adjustment Moderate social life, compensated for lack in one direction by activity in another	40	45	43
Some adjustment Meager social life, little contact with family, some emotional disturbance and discontent	22	11	16
Serious maladjustment Alone in the world, no friends, no reading or radio. Emotionally disturbed	0	4	2

for no individual rated at the top in all of them.

Analysis of the results indicated that good adjustment in the later years required a combination of the following eight characteristics: independence of and from the children, close companionship with the grandchildren, interest and pride in the great-grandchildren, home responsibilities, frequent contact with the kinship group, active participation in at least one social organization, regular church attendance, and active civic interests more than just casting a vote.

Discussion

The measurements showed that the majority of old people were still active and carried responsibility concentrated mainly in the home and in family relationships. Only moderate activity was found in social, church, and civic functions. Church memberships were not maintained by a few who had once belonged. No old people established their very first religious affiliation after 65. Memberships in organized groups had been dropped by some but many aged had never belonged to any clubs. Nonparticipation was for them not a result of aging but a carry-over from the earlier life pattern.

Active social participation in younger years seemed to lead to better adjustment in old age. However, high activity of any quality did not necessarily mean good adjustment in old age, for the aged who were still "running away" from something were not considered well adjusted. The facts indicated that well adjusted old people no longer competed for status positions of high office or responsibility but tended to withdraw to a more relaxed kind of participation as their strength and energy permitted. They concentrated their energy in family and home activities rather than outside this circle. Good family relationships in youth seemed almost a guarantee of happiness in old age. Well adjusted people without families tended to compensate by high social and civic activity started in youth or in the middle years.

This stratified representative sample included people in various stages of aging from the alert and active to the withdrawn and incapacitated old people. Most literature showed a biased sample based on Old Age Assistance recipients, residents of Homes for the Aged, or samples covering only one or two social status groups. The high degree of activity found in this study was due in part to the cross-sectional nature of the sample which included people in all social classes and all modes of life.

Summary

The distribution of role-activities and the social adjustment pattern of the aged were measured in a midwestern community. A proportional stratified sample of 100 subjects was selected for intensive study and included people of both sexes (45 men and 55 women), in all social classes, various marital status groups, and age-grades over 65.

The most common role-activities found inindicated that the majority of old people had the following patterns:

1. They were independent of their children. Eighty per cent of the fathers and 70 per cent of the mothers were neither responsible for nor dependent upon their children.
2. Grandparents participated socially with grandchildren in over 70 per cent of the cases, but 20 per cent of the men and 27.5 per cent of the women also took responsibility for them occasionally or part of the time.
3. Fifty-seven per cent of the great-grandparents participated socially with the fourth generation but tended to move toward communication without personal contact.
4. Old people who were parents rated higher than average in mean adjustment scores.
5. Home responsibility was shared with the spouse or another household member by 62 per cent of the aged.

6. Kinship relationships varied but 36 per cent were very active in visiting the extended family and only 3 per cent had no living relatives.
7. The majority, or 58 percent, belonged to no social clubs.
8. Only 47 per cent were constant and active church members.
9. Sixty-two per cent confined their civic activities to voting in the elections.
10. High role-activity ratings considered in this research were all significantly related to good adjustment.

The study presented in this paper is part of a dissertation for a Ph.D. degree from the University of Chicago.

References

1. Burgess, E. W., Cavan, R. S., and Havighurst, R. J.: *Your Activities and Attitudes.* Science Research Associates, Inc., Chicago, 1948.
2. Cavan, R. S., Burgess, E. W., Havighurst, R. J., and Goldhamer, H.: *Personal Adjustment in Old Age.* Science Research Associates, Inc., Chicago, 1949, pp. 128-131.
3. Merton, R. K., and Kendall, P. L.: The Focused Interview. *Am. J. Sociol., 51:* 541-557, 1946.
4. Warner, W. L., Meeker, M., and Eells, K.: *Social Class in America.* Science Research Associates, Inc., Chicago, 1949.

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The Role of the Professional Nurse in Community Planning for the Aged

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THE amazing changes in the age composition of our population and the rapidly increasing number of individuals who live to reach advanced years are by now familiar to every newspaper reader.

Professional nurses will find that several recent statistical tables published by Dr. Louis Dublin make this situation more easily comprehended. In table 1 we find the number of lives saved in the year 1947 as a result of the improvement in mortality since 1940. While the greatest gains are registered in the youngest group, the higher brackets show substantial advances, especially among women. When figures are available for the past two years more striking advances will surely be recorded as the result of the improved treatment of the infectious diseases of the elderly.

In table 2 we find the expectation of life and the chance of survival for white men and white women after the age of 65 years. These figures indicate vividly that today even after attaining the age of 75 years, a man or woman has a really worth while life expectancy.

These charts serve as an excellent introduction to a study of the role of the professional nurse in community planning for the aged, since her work today and in the future will be more and more centered on various aspects of the care of the aged. With advancing years

TABLE 1. NUMBER OF DEATHS IN THE POPULATION OF THE UNITED STATES IN 1947, BY AGE, COMPARED WITH THE NUMBERS EXPECTED IN THAT YEAR ON THE BASIS OF THE MORTALITY RATES BY SEX AND AGE PREVAILING IN 1940. (STATISTICAL BULLETIN, MAY, 1949; REPRODUCED BY COURTESY OF THE METROPOLITAN LIFE INSURANCE COMPANY).

AGE	MALES			FEMALES		
	DEATHS IN 1947		Lives Saved in 1947 by Improvement in Mortality Since 1940	DEATHS IN 1947		Lives Saved in 1947 by Improvement in Mortality Since 1940
	Actual[1]	Expected on Basis of Mortality in 1940		Actual[1]	Expected on Basis of Mortality in 1940	
ALL AGES	818,234	941,265	123,031	627,136	771,131	143,995
Under 1	68,678	111,912	43,234	50,579	82,357	31,778
1– 4	9,778	17,584	7,806	7,843	14,490	6,647
5–14	9,504	13,649	4,145	6,242	9,971	3,729
15–24	21,324	26,813	5,489	13,626	21,064	7,438
25–34	27,675	37,894	10,219	21,079	32,296	11,217
35–44	48,282	58,351	10,069	34,318	46,129	11,811
45–54	96,729	104,599	7,870	60,011	72,548	12,537
55–64	157,653	168,349	10,696	94,805	114,578	19,773
65–74	186,785	193,097	6,312	140,681	157,956	17,275
75 and Over	191,826	209,017	17,191	197,952	219,742	21,790

[1]Deaths of unknown age distributed.

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come not only the infirmities ascribed to the aging process itself, but also a variety of disease processes, many of which were formerly lumped under the all inclusive designation, "degenerative," which actually explained nothing. Today brilliant research is gradually making these conditions more comprehensible in terms of modern medical viewpoints. Thus, arteriosclerosis is now thought to be caused, in part at least, by a disturbance in fat metabolism, and many forms of crippling arthritis now seem to be related to endocrine disorders.

The entire community is deeply interested in the welfare of the aged not only as medical and nursing problems but also from economic, social, and political viewpoints. While our chief concern here is with question of health and disease in old age, we must ever realize that we are treating individuals and not diseases, that these human beings are products of varied environments, and that they live in close contact with other humans and are motivated in the strange ways characteristic of *homo sapiens.*

All our efforts must be based on the study of the individual and on the firmly held conviction of the dignity of the individual. In this way we shall be forced to busy ourselves with many questions not previously the concern of nurses, with housing and financial problems, with family disturbances, and with individual peculiarities. Every professional nurse owes it to herself, for her patients' sake, for her parents' sake, and finally for her own sake, as a preparation for her own later years, to seize upon every opportunity to learn as much as she can about the various effects of old age.

In a community program, therefore, the first objective is the education of physicians, of nurses, of social workers, and of the public. The second objective is the proper treatment

TABLE 2. EXPECTATION OF LIFE AND CHANCES OF SURVIVAL FOR WHITE MEN AND WHITE WOMEN AFTER AGE 65. UNITED STATES 1946. (STATISTICAL BULLETIN, OCTOBER 1948; REPRODUCED BY COURTESY OF THE METROPOLITAN LIFE INSURANCE COMPANY).

AGE	CHANCES PER 1,000 OF SURVIVING FROM BIRTH TO SPECIFIED AGE		CHANCES PER 1,000 AT AGE 65 OF SURVIVING TO SPECIFIED AGE		EXPECTATION OF LIFE YEARS	
	White Males	White Females	White Males	White Females	White Males	White Females
65	618	738	1,000	1,000	12.65	14.48
66	596	721	964	976	12.09	13.81
67	573	702	927	951	11.55	13.17
68	549	682	889	924	11.03	12.54
69	525	661	849	895	10.52	11.93
70	500	639	809	865	10.03	11.33
71	474	615	767	833	9.54	10.75
72	448	590	724	799	9.07	10.18
73	421	564	682	763	8.61	9.63
74	395	536	638	726	8.16	9.10
75	368	508	595	688	7.72	8.58

of the healthy and the sick aged in their homes and in appropriate institutions. The third objective is the establishment of preventive measures through a program of mental and physical hygiene. The functions of the professional nurse in striving for each of these goals are becoming clearer all the time and I have enjoyed the privilege of helping my nursing colleagues in the early stages of many such enterprises.

In the field of education many achievements have already been scored. Many worthwhile contributions to geriatric nursing have been published by leaders in the field, based on sound personal observations (1, 2, 9).

The Department of Nursing Education of Teachers College, Columbia University, began five or six years ago to send its students to the Home for Aged and Infirm Hebrews for a lecture demonstration on the nursing care of the aged. Today the program has grown into an official affiliation and a two weeks' attendance at the Home for lectures and demonstrations, besides work and special training in occupational therapy.

In the spring of 1949, an entire morning session of the annual institute of the New York City League for Nursing Education was held at the Home. Members of the medical, nursing, and social service staff gave informal talks to an audience of over 200 graduate nurses. The large attendance and the interest shown were striking evidence of the realization by the profession of the significance of rapidly advancing social and medical changes.

Two and one half years ago Miss Ollie Randall, Consultant on Old Age to the Community Service Society of New York, and the writer journeyed to Middletown, New York, for a conference on old age with the public health nurses of Orange, Rockland, and Sullivan counties. This was a memorable experience, since we learned at first hand the problems of the professional nurse engaged in public health work in rural areas. These women were keenly aware of the increasing number of aged coming into their sphere of influence, were taking measures to meet the challenge, and were eager to learn new techniques, new approaches, and new viewpoints. They were going about trying to set up recreation centers, special clinics, and special home services.

A textbook, "Geriatric Nursing", by Miss Kathleen Newton of New York Hospital has recently been published and deserves credit as the first in the field. It is well written and can be recommended to both students and graduate nurses (6).

In the field of undergraduate nursing education, encouraging progress is also being made. Following the spring meeting of the League at the Home, groups of student nurses from the Presbyterian Hospital and the St. Luke's Hospital Schools of Nursing have visited the Home for a tour of inspection and a talk by Miss Blanche Gubersky, our Director of Nursing (3). In time, no doubt, more stress will be placed in the curriculum of nursing schools on the physical and mental characteristics of the aged and how nursing care must be modified to meet these varying requirements. One can hardly overemphasize the importance of understanding the psychologic processes of the elderly, both normal and abnormal.

At this point there comes to mind the statement of the late William H. Matthews, who was a leader in establishing our modern attitudes. "If I were giving a Civil Service examination to persons who were to have the care of old people I would first try to find out whether they liked old people. If I discovered one who did not I should mark her so low that she would not be appointed. I did not mean by that I expected them to like equally every old person they met. I did mean that they must not have the attitude of mind which some people have that old age is a sort of chattering nuisance to be shoved around and kept out of one's way. People who do not like old folks, just because they are old, ought to stay away from them. In so doing they will save both themselves and the old people unhappiness" (5).

For private duty nurses as well as for those in general hospitals the increasing number of older patients bring new problems that press

for solution. Kresky and Luykx (4) reported nearly six years ago on the experience of the Third Medical Divisoon, Bellevue Hospital, New York, under the suggestive title, "The Patients are Older and Stay Longer"

In the Coordinated Hospital Service Plan of the United States Public Health Service the general hospital provides the aged with diagnostic service requiring complex procedures, as well as with therapy involving new or heavy equipment. Its psychiatric division will be called to furnish diagnostic and therapeutic service for elderly sufferers from mental disorders and to differentiate those requiring state hospital care from those for whom short term treatment may suffice. The responsibilities of the nursing services under this plan of organization will continue to grow in significance.

In hospitals for chronic disease where many of the patients are in the higher age groups and in the modern homes for the aged, where the aged are the objects of a careful program for maintaining their physical and mental health, the professional nurse must assume a new position of leadership by the side of the medical staff and must be capable of continuing development and increasing understanding (10). An important function here is the training of so-called "practical" nurses and attendants for a variety of duties.

The development of home care plans in connection with general hospitals and homes for the aged requires the active cooperation of the services of visiting nurses, who have long been aware of the large numbers of old people among the clientele. In such extramural medical programs the nurse works closely with the medical social worker, the visiting homemaker or housekeeper, and the visiting physician. Great importance today is being placed on the care of older patients in their own homes because it is psychologically desirable and economically unavoidable, since the number of needy elders is increasing far more rapidly than we can possibly provide institutional beds.

The present case load of the Visiting Nurse Service of New York has recently been made available to me through the courtesy of Miss Marian Randall, Director of the agency, and of Miss Mabel Reed, Statistician. In the first half of 1950 (January-June) nurses from their organization visited 4,000 patients 65 years of age and older. They made 53,000 visits to this group of aged patients. "During that period our field staff averaged 175 nurses, exclusive of those in supervisory positions. At present more than 75 per cent of all visits are made to sick persons and only one fourth to maternity, infant and other health supervision cases. Forty per cent of all morbidity visits (30 per cent of all visits) are made to patients at least 65 years of age. Two thirds of all morbidity visits (one half of all visits) are made to patients who have passed their fifty-fifth birthday" (7).

The urgency of the situation is nowhere more apparent than in state psychiatric hospitals where much of the overcrowding is due to the large numbers of old people whose advanced mental deterioration requires institutional care. Increased understanding is therefore required of the psychiatric nurse, but enlightened attitudes may in time make it possible to keep more of these old people out of the state hospitals.

Implicit in the education of the professional nurse is the stimulation of an optimistic attitude toward the ills of the old and the instruction in methods of the prevention of accidents, of infections, of premature cardiac breakdowns, and of malnutrition. The work of the New York University Institute of Rehabilitation under the leadership of Dr. Howard Rusk is directly applicable to the problems of the aged (8). Understanding of the basic principles involved is obligatory for the professional nurse and her wholehearted cooperation is indispensable.

That over-all community planning for the old in health and disease is an increasingly significant field for the professional nurse is well known to leaders in nursing education. It is important to realize that the impact of the aged on our social organization is such as to involve nurses in many varied fields of endeavor.

The community desperately needs the services that can be given only by the professional nurse in leadership, in education, in caring for the sick and the handicapped, and in the prevention of disease and infirmity.

Much of our effort to date in the field of old age has been limited to individual groups of workers or to special institutions. Often the general hospital is overlooked entirely and even today some writers on social welfare assign a secondary role to the physician. Such arbitrary division of activities can only do harm. The greatest measure of success in combatting a baffling and difficult problem can only be realized through coordinated efforts of public and private agencies and of medical, nursing, and social welfare organizations. These groups must in turn be associated closely with the research workers in the fields of biochemistry, physiology, nutrition, internal medicine, psychiatry, sociology, clinical psychology, and anthropology, for on these disciplines depend the developments of the future.

The role of the professional nurse in this large area of endeavor can hardly be overestimated, and every effort must be made to prepare personnel specially for this work. To do this will require broader educational foundations than ever before, and even the most vigorous critics of nursing education will have to admit the cogent social need for the professional woman thoroughly trained and carefully equipped for high endeavor in uncharted fields.

Summary

In this paper, addressed to professional nurses, the many ways in which they may participate in community efforts for the welfare of old people are outlined. Nursing educators are endeavoring to bring the necessary expert knowledge to both graduate and undergraduate students. A plea is made for greater cooperation between medical, nursing, and social service organizations in offering the best care to older individuals.

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References

1. Feamon, G.: Better Care for Older Patients. *Am. J. Nursing, 48:* 702-705, 1948.
2. Gellbach, S. B.: Nursing Care of the Aged. *Am. J. Nursing, 43:* 1112-1114, 1943.
3. Gubersky, B.: The Nursing Program of a Modern Home for the Aged. *Pub. Health Nursing, 41:* 582-584, 1949.
4. Kresky, B., and Luykx, H. M. C.: Patients are Older and Stay Longer. *Hospitals, 18:* 21-25, 1944.
5. Matthews, W. H.: *Adventures in Giving.* Dodd, Mead & Co., New York, 1939.
6. Newton, K.: *Geriatric Nursing.* C. V. Mosby & Company, St. Louis, 1950.
7. Personal communication.
8. Rusk, H. A., and Taylor, E. J.: *New Hope for the Handicapped.* Harper & Co., New York, 1949.
9. Smead, M. E.: The Older Nurse in Industry. *Am. J. Nursing, 43:* 1070-1071, 1943.
10. Zeman, F. D.: Medical Organization of the Modern Home for the Aged. *J. Gerontol., 5:* 262-266, 1950.

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PAUL D. WHITE: *Clinical Aspects* (Boston, Massachusetts)

EXCEPT for man's inhumanity to man, the greatest threat to health, happiness, and longevity in our so-called civilized countries today is, in all probability, arteriosclerosis. I would have you read arterial disease for arteriosclerosis since atheroma, in itself the precursor of sclerosis, may be even more serious. The veins though often seriously diseased threaten us less, with the exception of pulmonary embolism from leg vein thrombosis.

Innumerable thousands are crippled or killed by arterial disease in youth and middle age at the thresholds or even more often at the peaks of their useful careers. Time and again the history and forward progress of family, community, city, state, nation, or indeed of the world itself has been halted or changed by the dire effects of this disease on some important leader or group of leaders. It may also be, and I suspect that this is true too, that some unhappy events are avoided by a similar effect on the brain or heart of some malignant genius; of that we hear less although we now and then have our hopes.

The threat is a varied one, mostly cardiac to be sure, because of the involvement of the coronary circulation, and I would like to interpolate here the remark that the major volume of heart disease results from vascular causes, either coronary atherosclerosis or hypertension —there is very much less important primary heart disease which is nonvascular in origin. The brain, the kidneys, and the legs are also frequently crippled by arterial disease. The lesion may be very localized in almost any spot in the body, even doubtless in the memory center in the cortex defined recently by Penfield; I have myself encountered such a case, I believe, only the other day, an elderly man with nothing to be found wrong except for the sudden onset, for unknown reason, of a loss of memory.

Thus, today one needs no excuse for concentrating research in the field of arteriosclerosis. There is far too little as yet. Indeed it has been surprising that this most important disease of all has been so slow in being taken up as a challenge for research. I suppose that three of the reasons have been 1) that it has been considered chronic (without appreciation of the fact that it may begin as a serious acute process), 2) that it is predominantly in older persons, and most young persons, that is, under 40, are likely to regard it rather a waste of time to study or treat persons over 70, and 3) that it is irreparable and viewed as God's will.

After these introductory remarks I would like to cite briefly a few ways in which the clinical aspects of arteriosclerosis, which can yield important clues as to the etiologic factors, may be clarified by further researches. The results of such studies may help to point out the directions in which more fundamental investigations both in animals and in man may be more wisely pursued.

First, then, we should know, better than we know today, the actual frequency of important manifestations of arteriosclerosis, not only in old age but also in youth and middle age in this country. We need to do some extensive and intensive case finding in which there should be a happy blending of private enterprise (by way of private practitioners of medicine and private agencies such as local heart associa-

tions, state medical societies, and research groups in medical schools and teaching hospitals) with public enterprise (by way of state and federal grants of funds and a supply of workers when needed to assist in such investigations).

We have but vague ideas and inadequate statistical knowledge of the actual incidence of arteriosclerosis involving heart, brain, kidneys, or legs in supposedly healthy men, say 50 years old, throughout the breadth of this country today. I was not unduly surprised the other day to read in an article, by reliable observers, of the electrocardiographic findings in persons over 45 years of age with angina pectoris and in a control series of 100 persons over 45 years of age without any other evidence of heart disease, that 15 per cent of the control group showed abnormal records, for the most part doubtless due to otherwise silent coronary heart disease. We need careful studies of thousands of such control cases as well as of the obviously sick ones.

A second opportunity that awaits us is related to the first but is more promising as to etiologic clues. It is an obviously needed study and has been frequently referred to in recent years by myself and others. It requires, however, much planning and implementation, best I suppose on community, state, interstate, national, and international levels. It is to be, we hope, one of the functions of the new International Society of Cardiology founded in Paris two months ago. It consists of a comparison of the cardiovascular findings in large groups of the population differing in one or more characteristics, such as diet (including a possible effect from religious fasting and feasting), occupation, customs, climate, body build, sex, heredity, and race.

The two most clearcut clues as to coronary artery atherosclerosis which we possess already but the explanation of which we still lack are 1) that under the age of 40 coronary heart disease affects the male sex in an extraodinary proportion (in a study of 200 such cases in Boston there were 193 men and only 7 women), and 2) that it is the mesomorph (the person of preponderantly muscular build) in contrast to the ectomorph (one of thin build) or endomorph (one of rotund build) who is most likely to be the victim of serious coronary atherosclerosis in youth.

Extensive research as to the relative importance of other factors will be, admittedly, often a difficult task because of the frequent combinations of such factors, but it should by no means be insuperable. At present there are only rarely statistically and scientifically adequate observations about these comparisons; mostly there are merely theories or rumors or guesses. Results of animal experimentation, valuable though it be and of fundamental importance, cannot always be applied to man or even to other species of the animal kingdom, as witness some of the discussion to which I listened at the interesting meeting of the American Society for the Study of Arteriosclerosis in Chicago a week ago this morning. Neither can we always duplicate in animals the lesions in man, who lives longer than most animals. Nor can we justifiably experiment on man except in a benign way.

Thirdly, we can study more than we have in the past the effect of various disease processes as a possible background for arteriosclerosis in man. We already know that diabetes mellitus, severe chronic hypertension (either systemic or pulmonary), xanthomatosis, and syphilitic aortitis favor the superimposition of arteriosclerosis, but the majority of cases of presenile arteriosclerosis apparently have had none of these diseases. It was of interest to Dr. Glendy, Dr. Levine, and myself some ten or twelve years ago that a group of several hundred healthy persons over 80 years old had had in their youth much more serious infectious disease such as diphtheria, scarlet fever, and typhoid fever, than had a group of 100 persons who developed coronary heart disease before the age of 40, many of whom had had almost nothing in the way of apparently important infections.

Finally, I shall refer to one other clinical aspect of arteriosclerosis which might profitably be explored though there are doubtless

still others of equal or greater importance. For a long, long time, dating back to the time of Hippocrates or beyond, there have been therapeutic and prophylactic measures, based on empiricism alone, recommended for the prolongation of life, in part I dare say through retardation of the development of arteriosclerotic changes, that deserve at least mention. Such measures include the prescriptions of regulated exercise, rest, entertainment, diet, and mineral water, inside and out, at the ancient asklepia in Greece and spas from Roman days down to our own.

A so-called "cure" lasting three weeks even only once a year may conceivably increase a healthy longevity in the case of the average business or professional man of modern times who is so harassed by the pressure of life today that he never thinks that he has time for relaxation, physical or mental, or for a proper use of the musculature, often abundant, with which he is endowed, although he continues to eat heartily.

Perhaps a proper use of his muscles by the mesomorph, who is a candidate for early coronary atherosclerosis of serious degree, is more important than his diet. Muscular metabolism, in large part neglected in current studies, may be as important as the metabolism of fat, and in particular of cholesterol, in relation to presenile arteriosclerosis or indeed to senile arteriosclerosis. Only the other day I examined a healthy and lively old gentleman, aged 100 years the week before, and found no evidence of arteriosclerosis except for a slightly abnormal electrocardiogram; he began to work at the age of 11, retired at the age of 93 but has continued to be as physically active and lively as he has been all his life. There is an old German saying:

> Wenn mann weiss nicht wieso, warum,
> Dann gibt mann gleich Iodkalium.

Do the iodides or thyroid extract retard the development of arteriosclerosis? Thyrotoxicosis seems to be protective in that respect, but is there anything in these drugs or others such as choline and lecithin that do really help? In foreign lands there are doubtless old traditions of the protective influence of one or another ancient food, drug, or custom from which clues might come. There has been a current revival of the use in this country of the yogurt (or yaourt) of the Near East along with black strap molasses, and brewer's yeast that sounds almost as unpalatable as the rice diet.

Let me close with a confession of tardiness of insistence by some of us clinicians working in the cardiovascular field of the urgency of research about arteriosclerosis. Leary, Anitschkov, and a few other pathologists like them were as prophets crying in the wilderness beseeching us to do something about it. Only the pressure of the magnitude of the problem today, based in part on the effectiveness of the many workers in the field of the infectious diseases, in particular infantile dysentery, diphteria, and tuberculosis in childhood and typhoid fever and pneumonia in youth, and now we may hope streptococcus sore throat and rheumatic fever, has forced our hand. Happily the challenge has been accepted and it seems obvious to me that the more numerous the well trained workers whom we can put on the job in well equipped clinics and laboratories with ample freedom to work at their own bright ideas, as well as in cooperative studies, the sooner we shall be making real headway in meeting the challenge which incidentally concerns old people as well as our youth and middle aged.

I would finish by quoting from a recent article by Best published by the Federation of American Societies for Experimental Biology: —"We hope and expect that those whose most vigorous and productive years in research lie in the second half (of the twentieth century) will explain many 'intimate actions' which we have left unsolved".

W. STANLEY HARTROFT: *Experimental Renal Hypertension of Dietary Origin*
(Banting and Best Institute of Medical Research, University of Toronto, Toronto, Canada)

THE paths by which investigators have approached the field of vascular disease are many. That followed in our laboratories at the University of Toronto originated with the successful isolation of insulin by Banting and Best. When sufficient insulin became available for long-term investigations, it was demonstrated (1, 5) that despite adequate treatment of the diabetes of depancreatized dogs with insulin, their livers became very fatty.

A series of further experiments established that the oral administration of *choline* would not only prevent the accumulation of excess fat in the livers of these animals (2, 6, 28), but also correct the condition once it had developed. This finding was subsequently extended to normal rats by Best and his associates (30), and it is now known that the presence of an adequate supply of lipotropic factors in the diet—choline or its precursors, methionine and betaine—is necessary to prevent fatty change in the livers of not only dogs and rats, but also many other species.

The available evidence indicates that this also applies to man. It is now known beyond question that the fatty liver of dietary choline deficiency may be followed by the development of grossly nodular cirrhosis (7, 10, 11, 15, 18, 25). Experiments conducted in this laboratory have suggested that the frequent association of cirrhosis with habitual and excessive consumption of alcoholic beverages may be explained by a relative deficiency of lipotropic factors (4).

In 1939, Griffith and Wade (17) reported that a deficiency of choline in the diet of weanling rats not only caused their livers to become very fatty, but also rapidly (within seven to ten days) led to an acute fulminating renal lesion, most often fatal to the animal. These authors described associated changes in other organs (ocular haemorrhages, thymic atrophy, adrenal cortical enlargement) and included all these lesions in the term "haemorrhagic renal syndrome."

The reports from our laboratory (3, 27) that a persistent and severe degree of hypertension may develop in rats fed a normal diet for three to four months after they have survived the haemorrhagic renal syndrome have now been confirmed by other investigators (9, 20, 31). The type of renal damage produced in the young animals by choline deficiency will first be described, and the lesions in the vessels and kidneys associated with the development of hypertension in the later life of survivors will then be considered. Finally, some of the factors which may elevate blood pressure in these animals will be indicated.

Acute renal damage in young rats produced by a dietary deficiency of choline.—Christensen (12, 13) has described the pathology of the renal lesions responsible for the death of weanling rats (35 to 42 gm.) which may result from an acute deficiency of dietary choline. Grossly the kidneys appear red, smooth, and very swollen; in fact their weights may increase to twice normal. Necrosis of groups of tubules in the cortex is the most important finding on microscopic examination. Capillaries in some regions are compressed by the swollen parenchyma and in others are distended with blood. Areas of haemorrhage are found within and beneath the layers of the renal capsule. Lesions of the glomeruli range from acute congestion to frank necrosis, but these structures are not so uniformly involved as the tubules, and in many cases glomerular necrosis may be limited to the outer third of the cortex. Epithelium of medullary tubules is relatively unaffected, but their lumina are filled with innumerable eosinophilic casts of a colloid nature, and these constitute a prominent feature of the microsections.

The pathogenesis of these renal lesions has been studied in this laboratory (24, 26). His-

tologic observation of the kidneys of weanling rats, groups of which were killed at daily intervals while fed a choline-deficient diet, demonstrated that renal cortical necrosis was the result of the following series of events. Within the first day or two after the animals were started on the basal diet, many small droplets of stainable fat made their appearance within the cytoplasm of the epithelium of the proximal convoluted tubules. As the lesions progressed, the amount of sudanophilic lipid in many of the tubules became increasingly great. This was accompanied by a simultaneous swelling of the tubule-cells which contained lipid.

At this stage, special cleared preparations to demonstrate the renal vasculature, which had been injected with india ink, revealed a significant reduction in the diameters of the cortical capillaries in the peripheral and subcapsular portions of each renal lobule. Further study of these and other microsections provided evidence that swelling of fatty tubules was responsible for this compression of intertubular capillaries of the terminal portions of the lobular vascular tree.

For convenience, this chain of events has been designated "TOC" (tubular obstruction of capillaries). The ischaemia produced by TOC was found responsible for the tubular necrosis. The capillary bed, proximal to the regions where it became obstructed, was distended with arrested blood, but haemorrhage occurred only in those sites where swollen tubules did not support the vessels on all sides, i.e., beneath the capsule. This haemorrhage, consequently confined to subcapsular regions, is responsible for the characteristic gross appearance of the organs.

Necrotic debris from tubules in the cortex became washed into the lumina of those in the medulla where it was precipitated in the form of eosinophilic casts. Photomicrographs to demonstrate this and other supporting evidence have been published elsewhere (24). The pathology of the ocular, thymic, and adrenal lesions has been carefully studied (8, 14, 16, 32), but will not be discussed here, as their relation to hypertension in rats which survive the syndrome is not evident at present.

Renal and vascular lesions associated with hypertension which develops within three to five months in survivors of the haemorrhagic renal syndrome which have been fed normal diets.—In the experiments reported from this laboratory (27), the death of many of the young rats in which the renal haemorrhagic syndrome had been produced was prevented by replacing the choline-deficient diet after five to six days with a normal stock ration. In slightly over 50 per cent of 62 such survivors, hypertension developed within three to five months. None of these animals were considered hypertensive unless the average of systolic and diastolic levels of blood pressure measured by a direct method was higher than 150 mm. Hg., (the average figure for 36 controls was 118 mm. Hg.). The degree of cardiac hypertrophy and the severity of renal and vascular lesions found at autopsy varied directly with the level of blood pressure.

In contrast with the striking tubular lesions which were found in the kidneys of those animals which died from the acute effects of the haemorrhagic renal syndrome, the changes which were most prominent in microsections of kidneys of the hypertensive rats were present in the glomeruli. Their number was greatly reduced, and those which remained varied in size all the way from small atrophic structures in the subcapsular zones to others situated more deeply within the cortex which were hypertrophied—some even to such a degree that they were twice the normal in diameter.

Nearly all glomeruli were found affected to some extent by pericapsular fibrosis and by hyalinization of the capillary loops. The tubules of both cortex and medulla were similarly affected in that all extremes from sclerotic atrophy to hypertrophy were encountered; some were greatly distended and filled with intensely eosinophilic casts. Tubules of the latter type, when cut in cross section, sometimes presented an appearance which in a re-

markable manner closely resembled that of thyroid follicles.

Counterparts of the vascular lesions which characterise cases of both benign and malignant phases of hypertensive disease in man were found in the kidneys of the hypertensive rats. Cellular hyperplasia of adventitial and muscular layers of many of the arterioles had produced an appearance which resembled the layers of an "onion-skin". Subendothelial deposits of eosinophilic hyaline material had narrowed the lumina of others. In a small number of animals in which the blood pressure had attained levels of 190 mm. Hg. or over, and in which renal damage had been sufficient to produce impairment of excretory function, fibrinoid necrosis of the arterioles was present. These latter lesions were identical with the arteriolar necrosis found in the malignant phase of hypertension in man.

Cleared slices of kidneys of hypertensive rats which had been injected intravascularly with india ink served to demonstrate the extent to which the glomerular vascular bed had been reduced, and the degree to which this had occurred in any one animal was clearly correlated with the height of its blood pressure at the time it was sacrificed. For this reason it was suggested that this reduction in the capacity of the glomerular vascular bed might be considered a crucial factor in the pathogenesis of hypertension in these rats. Doubtless other factors of equal or even greater importance are also involved, and these will be indicated in the final section of the paper.

At least two processes are concerned with the pathogenesis of the renal lesions which were encountered at autopsy of the hypertensive animals. Evidence of the irreversible changes in nephrons which had occurred during the acute period of choline deficiency still stigmatised these kidneys months later when the rats were killed. Deposits of haemosiderin pigment and of calcium salts in the subcapsular zones and in some of the atrophic tubules probably originated in this manner. On the other hand, glomerular sclerosis and arteriolar thickening were more likely the direct result of the hypertension, *per se, once* it had become established.

Histologic studies of animals sacrificed at intervals during the latent period at the time of recovery from the acute renal damage, but prior to the onset of hypertension, have indicated that renal lesions at this stage are not prominent. The most striking alterations in glomeruli and tubules which escape destruction during the acute period occur after the level of blood pressure is found to have risen. Lysis of tubules and glomeruli which are destroyed by necrosis is so complete as to leave only inconspicuous traces of the true extent of the damage.

But as the *nephrogenic* zone (23) at the renal periphery is that which has been subjected to the greatest degree of injury, there is disturbance of the usual physiologic hypertrophy and hyperplasia of nephrons which occurs chiefly in this region as a concomitant of normal renal development during the period in the rat's life which would correspond to adolescence in man. The growth rate of the kidneys is accordingly impaired, but as the animals are being fed a normal diet, the rate of gain in total body weight approaches that of normal controls.

It is suggested that the resultant imbalance between the speed of maturation of the animal as a whole and of its kidneys is an important factor in the aetiology of the hypertension which manifested itself by the time these rats had attained sexual maturity.

Factors responsible for the elevation of blood pressure in dietary hypertension.—In addition to those factors which have been suggested above, there is much evidence that others of equal importance are involved, and these will now be considered. Before it was discovered that hypertension could be produced in survivors of the haemorrhagic renal syndrome by transferring them to a normal diet, it had been shown that the levels of blood pressure remained within normal limits in rats maintained on choline-deficient rations for periods of several months (29, 33).

Although renal damage of a chronic type develops only slowly in these animals, it may finally attain a degree comparable to that encountered in the hypertensive rats. Unpublished data obtained in our laboratories have indicated that despite the absence of hypertension in rats with advanced chronic lesions of this type, there is a significant increase in their cardiac weights. Cirrhosis is frequently severe in these rats, but even in a few in which the liver had escaped any appreciable amount of damage hypertension was absent.

These nonhypertensive animals, which had been subjected to long periods of dietary choline deficiency, differed from the hypertensive rats in that they were invariably thin and underdeveloped—and it was apparent that this would have minimised any tendency towards an imbalance between the rate of gain in body weight and of renal growth. However, the necessity for considering certain hormonal factors and the composition of the diet in any attempt to explain the above data has been shown by the recent experiments reported by Handler and Bernheim (19, 20, 21, 22).

These investigators found that hypertension in survivors of the haemorrhagic renal syndrome could be abolished if they were fed synthetic diets low in either protein or salt instead of normal rations. They also demonstrated that the hypertension produced in rats by subtotal nephrectomy could be eliminated by feeding the animals a choline-deficient diet. Elevation of blood pressure recurred if adrenocorticotrophic hormone was administered to these animals, but this procedure had no effect on the blood pressures of choline-fed controls. The depressor effect of a choline-deficient diet was present even when the level of protein was kept within normal limits.

The addition of choline in excessive amounts had been shown to exert a pressor effect when added to low-protein diets, but a pharmacologic effect may be involved here. A supplement of 0.35 per cent choline chloride, when added to the choline-deficient diet of animals in which the chronic type of renal damage had been produced, failed to elevate their blood pressure in experiments conducted in this laboratory (unpublished data). The depressor effect of low-protein or choline-deficient diets in Handler and Bernheim's experiments was considered by these authors to be mediated through the anterior pituitary since the administration of epinephrine produced only one-half as great a decrease in the eosinophile count as occurred in control animals similarly treated.

This brief discussion has probably only served to a limited extent to indicate some of the gaps in our knowledge of the factors responsible for the production of experimental dietary hypertension by the procedures described in the first half of this paper. Accurate evaluation of the relative importance of the roles played by renal damage, growth rate, hormonal production by the anterior pituitary and the adrenal cortex, and the composition of the diet cannot be attempted until the necessary data have been provided by further investigations of the type already completed by Handler and Bernheim.

In conclusion, it should be emphasised that the production of the acute haemorrhagic renal syndrome in any experimental animal other than the young rat has not been achieved. Any attempt therefore to apply the results of these investigations to the field of clinical medicine cannot be justified at the present time. To the geraeologist, however, the demonstration that the experimental counterpart of a disease commonly associated with late life may have its origin in a brief, acute episode in childhood should be of interest. It is possible that a similar approach to the problems confronting the investigator of other disorders commonly associated with old age, such as cancer or diabetes, might prove rewarding.

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References

1. Allan, F. N., Bowie, D. J., MacLeod, J. J. R., and Robinson, W. L.: Behaviour of Depancreatized Dogs Kept Alive with Insulin. *Brit. J. Exper. Path.*, *5*: 75-83, 1924.

2. Best, C. H., Ferguson, G. C., and Hershey, J. M.: Choline and Liver Fat in Diabetic Dogs. *J. Physiol., 79:* 94-102, 1933.
3. Best, C. H., and Hartroft, W. Stanley: Nutrition, Renal Lesions and Hypertension. *Federation Proc., 8:* 610-617, 1949.
4. Best, C. H., Hartroft, W. S., Lucas, C. C., and Ridout, J. H.: Liver Damage Produced by Feeding Alcohol or Sugar and Its Prevention by Choline. *Brit. Med. J., ii:* 1001-1006, 1949.
5. Best, C. H., Hershey, J. M., and Huntsman, M. E.: The Control of the Deposition of Liver Fat. *Am. J. Physiol., 101:* 7, 1932.
6. Best, C. H., and Huntsman, M. E.: The Effect of the Components of Lecithine upon Deposition of Fat in the Liver. *J. Physiol., 75:* 405-412, 1932.
7. Blumberg, H., and McCollum, E. V.: Prevention by Choline of Liver Cirrhosis in Rats on High-Fat, Low-Protein Diets. *Science, 93:* 598-599, 1941.
8. Burns, J. Lloyd, and Hartroft, W. Stanley: Intraocular Haemorrhages in Young Rats on Choline-Deficient Diets. *Am. J. Ophthal., 32:* 79-91, 1949.
9. Campbell, Moses: Production of Hypertension Following Choline Deficiency in Weanling Rats. *Am. J. Physiol., 163:* 736, 1950.
10. Chaikoff, I. L., and Connor, C. L.: Production of Cirrhosis of the Liver of the Normal Dog by High Fat Diets. *Proc. Soc. Exper. Biol. & Med., 43:* 638-641, 1940.
11. Chaikoff, I. L., Connor, C. L., and Biskind, G. R.: Fatty Infiltration and Cirrhosis of the Liver in Depancreatized Dogs Maintained with Insulin. *Am. J. Path., 14:* 101-110, 1938.
12. Christensen, K. A.: Microscopic Study of the Effect of Choline Deficiency in Young Rats. *J. Biol. Chem., 133,* xx, 1940.
13. Christensen, K.: Renal Changes in the Albino Rat on Low-Choline and Choline-Deficient Diets. *Arch. Path., 34:* 633-646, 1942.
14. Christensen, K., and Griffith, W. H.: Involution and Regeneration of Thymus in Rats Fed Choline-Deficient Diets. *Endocrinology, 30:* 574-580, 1942.
15. Connor, C. L., and Chaikoff, I. L.: Production of Cirrhosis in Fatty Livers with Alcohol. *Proc. Soc. Exper. Biol. & Med., 39:* 356-359, 1938.
16. Deane, H. W., and Olson, R. E.: Stimulation of the Zona Glomerulosa of the Rat's Adrenal Cortex Associated with the "Haemorrhagic" Kidney of Choline Deficiency. *Anat. Rec., 100:* 21, 1948.
17. Griffith, W. H., and Wade, N. J.: Choline Metabolism. I. The Occurrence and Prevention of Hemorrhagic Degeneration in Young Rats on a Low Choline Diet. *J. Biol. Chem., 131:* 567-577, 1939.
18. György, P., and Goldblatt, H.: Hepatic Injury on a Nutritional Basis in Rats. *J. Exper. Med., 70:* 185-192, 1939.
19. Handler, P., and Bernheim, F.: Importance of Dietary Protein, Calories and Salt in Experimental Renal Hypertension. *Am. J. Physiol., 160:* 31-40, 1950.
20. Handler, P., and Bernheim, F.: Influence of Dietary Protein in Hypertension Induced by Choline Deficiency. *Am. J. Physiol., 162:* 189-192, 1950.
21. Handler, P., and Bernheim, F.: Physiological Basis for Efforts of Low-Protein Diets on Blood Pressure of Subtotally Nephrectomized Rats. *Am. J. Physiol., 162:* 368-375, 1950.
22. Handler, P., and Bernheim, F.: Effect of Choline Deficiency on ACTH Production and on Hypertension of Subtotally Nephrectomized Rats. *Am. J. Physiol., 162:* 375-378, 1950.
23. Hartroft, W. Stanley: The Vascular Development of the Kidney of the Pig. *Tr. Roy. Soc. Canada (Sect. V, Biol. Sc.), 35:* 67-80, 1941.
24. Hartroft, W. Stanley: Pathogenesis of Renal Lesions in Weanling and Young Adult Rats Fed Choline-Deficient Diets. *Brit. J. Exper. Path., 29:* 483-494, 1948.
25. Hartroft, W. Stanley: Accumulation of Fat in Liver Cells and in Lipodiastaemata Preceding Experimental Dietary Cirrhosis. *Anat. Rec., 106:* 61-88, 1950.
26. Hartroft, W. Stanley, and Best, C. H.: Lipoid Substance in the Cells of Proximal Convoluted Tubules of the Kidneys of Young Rats on a Choline-Deficient Diet. *Science, 105:* 315-316, 1947.
27. Hartroft, W. Stanley, and Best, C. H.: Hypertension of Renal Origin in Rats Following Less than One Week of Choline Deficiency in Early Life. *Brit. Med. J., i:* 423-426, 1949.
28. Hershey, J. M., and Soskin, S.: Substitution of "Lecithin" for Raw Pancreas in the Diet of the Depancreatized Dog. *Am. J. Physiol., 98:* 74-85, 1931.
29. Honorato, C., and Vadillo, N. I.: Dieta sin Colina y Presion Arterial en Ratas. *Rev. de med. y aliment., 6:* 143-145, 1944.
30. MacLean, D. L., and Best, C. H.: Choline and Liver Fat. *Brit. J. Exper. Path., 15:* 193-199, 1934.
31. Merritt, Phyllis: The Effect of a Deficiency of the B Vitamin Complex (Except Thiamine) on the Blood Pressure of the Rat. *J. Exper. Med., 92:* 333-336, 1950.
32. Olson, R. E., and Deane, H. W.: A Physiological and Cytochemical Study of the Kidney and Adrenal Cortex During Acute Choline Deficiency in Weanling Rats. *J. Nutrition, 39:* 31-56, 1949.

33. Sobin, S. S., and Landis, E. M.: Blood Pressure of the Rat During Acute and Chronic Choline Deficiency. *Am. J. Physiol., 148:* 557-562, 1947.

HENRY S. SIMMS: *A Review of Research on Lipfanogens and Antilipfanogen* (Department of Pathology, College of Physicians and Surgeons, New York, New York)

THE effect of agents present in adult blood plasma on the deposition of fat in adult artery tissue cultures has been studied over a period of years (1, 2, 3, 4). There is definite evidence that the following agents are present in blood plasma:

1. *Ether-soluble free lipfanogens,* and
2. *Ether-insoluble free lipfanogens.* The lipfanogens (substances producing visible fat) are special heat-stable lipoid substances that are taken up by living cells and converted into visible fat. These lipfanogens include both ether-soluble stances and ether-insoluble material (perhaps lipoproteins). They are found not only in plasma but in various tissues. They are stable at 100 C. They are not necessarily high in cloudy serum.
3. *Combined lipfanogens and antilipfanogen.* This complex does not produce fat deposition. Only the free uncombined lipfanogens cause the deposition of fat.
4. *Free Antilipfanogen. Antilipfanogen* is an opposing agent which reduces or prevents fat deposition. It is present in blood plasma and seems to form an inactive complex with the lipfanogens. The formation of this complex obeys the following equilibrium equation:

$$k = \frac{[\text{Free Antilipfanogen}]\,[\text{Free Lipfanogens}]}{[\text{Lipfanogen-Antilipfanogen Complex}]}$$

Antilipfanogen is found in the serum albumin fraction (Cohn's Fraction V) but not in significant amounts in tissue extracts. It has been separated in concentrated form and further work on its isolation is in progress. Antilipfanogen is destroyed by heating at 80 C.

5. *Precursors.* These substances in blood plasma do not in themselves cause fat deposition but, on incubation at 37 C. (in the presence of an enzyme also in plasma) are converted into free lipfanogens. Heating at 100 C. kills the enzyme and stops the conversion.

Determination of Activity

In order to determine the concentrations of lipfanogens and antilipfanogen in a given sample of serum, tissue cultures of adult chicken aorta fibroblasts are specially prepared in such a way that they are free from fat granules. Three separate cultures are then treated with solutions containing portions of serum which have been: 1) unheated, 2) heated at 80 to 100 C., and 3) incubated three days, then heated at 80 to 100 C. The total amount of lipfanogens, free plus bound, (expressed on an arbitrary scale proportional to the concentration, with normal values of about 30 units and in extreme cases up to 70) is indicated by the extent of fat granule formation produced by the heated serum (portion 2). The amount of antilipfanogen (free, combined, and total) is computed from the fat granule production of the first two solutions. The amount of precursor is represented by the difference between the fat granule production of the second and third solutions.

Relation to Arteriosclerosis

The following evidence indicates that the lipfanogens are involved in the fat deposition of atherosclerosis and that antilipfanogen serves to prevent this deposition, so that the tendency toward fat deposition is controlled by

the relative amounts of antilipfanogen and of lipfanogens:

1. Segments of adult chicken innominate arteries incubated in a medium containing lipfanogens developed deposits of stainable fat strongly resembling the type of deposits seen in spontaneous chicken atherosclerosis.
2. Segments of human splenic arteries, similarly treated, developed slight stainable fat in the intima suggestive of early human lesions. Careful controls were run in all cases, each alternate segment serving as a control.
3. In a series of studies on human serum it was found that the ratio of free lipfanogens to free antilipfanogen was slightly lower in females than in males, the average being about 0.92.
4. This free L/A ratio was found to be high in the serum in diabetes (1.57), in coronary disease (2.09), and in nephrotic syndrome (2.62). The same sera were high in cholesterol and other lipoids. The data are summarized in table 1.
5. Studies on sera from different species showed that those having low incidence of atherosclerosis had a low total L/A ratio (such as horses 0.6, and dogs 0.5). Conversely, chickens, with prevalent atherosclerosis, had a high ratio (2.0).
6. Thyroid extract given by mouth caused an immediate increase in the antilipfanogen in the serum.

It has been found, furthermore, that in a given individual, the ratio of total lipfanogens/antilipfanogen remains remarkably constant while both these agents fluctuate from day to

TABLE I. OBSERVATIONS ON LIPFANOGENS AND ANTILIPFANOGEN IN NORMAL INDIVIDUALS AND PATIENTS SUFFERING FROM VARIOUS DISEASES

	Normal Individuals	Diabetes	Coronary Disease	Nephrotic Syndrome
No. and Sex	5M, 10F	7M, 13F	15M, 12F	7M, 13F
Mean Age	27	46	53	41
Fat Regulators:				
L_F = Free Lipfanogens	7.6	9.3	9.4	8.2
ΔL = Bound Lipfanogens	21.8	16.2	13.9	11.0
L_T = Total Lipfanogens	31.6	26.7	23.3	19.3
P = Precursor	11.3	7.5	13.2	14.8
$A_F = A_T - \Delta L$ = Free Antilipfanogen	8.3	5.9	4.5	3.1
A_T = Total Antilipfanogen	32.2	22.7	18.4	14.1
L_F/A_F = Free Ratio	0.92	1.57	2.09	2.62
L_T/A_T = Total Ratio	0.97	1.16	1.30	1.57
Serum Lipoids:				
Total Lipoids	846	1305	1137	1417
Phospholipoids	189	282	270	286
Cholesterol				
Free	53	81	82	92
Ester	145	209	195	214
Total	198	290	277	306
Other Lipoids	458	733	590	825

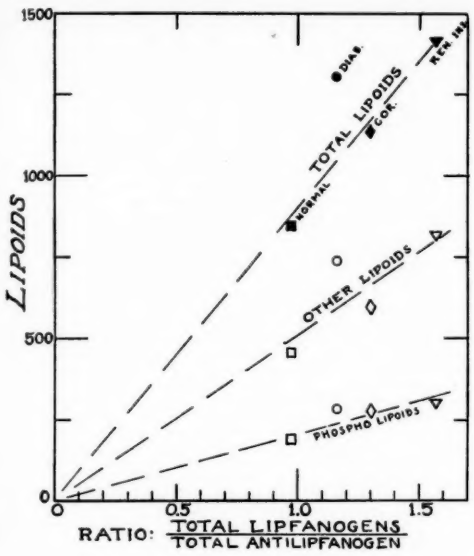

FIG. 1

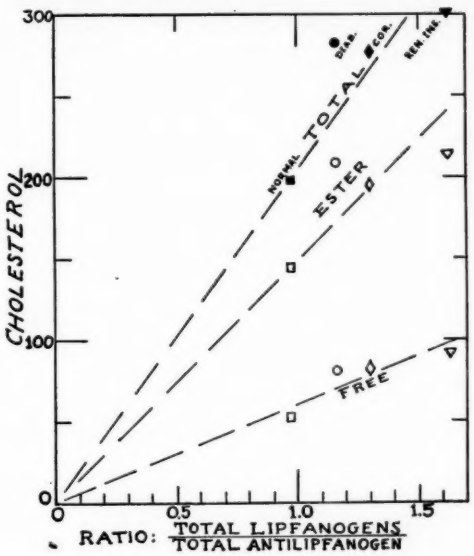

FIG. 2

day. It is therefore believed that the L/A ratio is important. The conditions involved in regulating the ratio are being studied. It will be observed in figures 1 and 2 that the total L/A ratio is roughly proportional to the various serum lipoids. The body may have some mechanism for eliminating the excess free lipfanogens, thus maintaining a constant ratio. However, present studies on liver disease have not indicated that the liver serves this function.

Relation to Hypercholesterolemia

It is well known that in conditions associated with high incidence of arteriosclerosis there is high serum cholesterol, phospholipoids, and other lipoids. We also know that the L/A ratio is high in these sera. The relationship between these phenomena has not been determined, but there are indications that the high serum lipoids may combine with antilipfanogen and render it unavailable for inactivating the lipfanogens. It will be noted in table 1 that with increasing serum lipoids there is a drop in total lipfanogens, but a rise in *free* lipfanogens.

Cholesterol Deposition

Very early atheromatous lesions are typified by a predominance of neutral fat, while cholesterol is not observed to predominate, either visibly or by chemical analysis, until the lesions are more advanced. It is therefore suggested that (a) free lipfanogens may play the important role in the fat deposition, (b) cholesterol may enter the deposits along with the lipfanogens (either in solution or as part of the lipfanogen molecules), and (c) the neutral fats are subsequently metabolized, leaving an accumulation of cholesterol.

Summary

Tissue culture studies have shown that blood plasma contains: (1) ether-soluble, and (2) ether-insoluble, free lipfanogens that are converted by living cells into visible fat deposits, (3) an inactive complex of lipfanogens combined with antilipfanogen, (4) free antilipfanogen, in equilibrium with the complex, and (5) precursors that, on incubation, are converted into lipfanogens.

As evidence that these agents serve to regulate the fat deposition in atherosclerosis, it is pointed out that fat deposits have been produced in chicken and human arteries in vitro by the action of lipfanogens and that the free lipfanogens (as well as their ratio to antilipfanogen) are high in those conditions and species associated with high incidence of atherosclerosis, whereas free lipfanogens (and the ratio) are low in species having little or no atherosclerosis. A theory is suggested to explain how hypercholesterolemia may upset the lipfanogens/antilipfanogen balance and thereby be an indirect cause of atherosclerosis.

It is suggested that cholesterol deposition may occur in conjunction with lipfanogens rather than as a direct deposition.

This investigation has been conducted in the Department of Pathology of the College of Physicians and Surgeons (Columbia University) with the cooperation of Dr. Kenneth B. Turner in the Department of Medicine. It has been aided by grants from the National Heart Institute of the National Institutes of Health of the U.S. Public Health Service, the Josiah Macy, Jr. Foundation, the Albert and Mary Lasker Foundation, the New York Heart Association, and the Life Insurance Medical Research Fund.

References

1. Simms, Henry S., and Stillman, Nettie P.: Production of Fat Granules and of Degeneration in Cultures of Adult Tissue by Agents from Blood Plasma. *Arch. Path., 23:* 316-331, 1937.
2. Simms, Henry S., and Stillman, Nettie P.: Fat Deposition in Arteries Treated in Vitro with the B Factor. *Arch. Path., 23:* 332-337, 1937.
3. Simms, Henry S., and Sanders, Murray: Use of Serum Ultrafiltrate in Tissue Cultures for Studying Deposition of Fat and for Propagation of Viruses. *Arch. Path., 33:* 619-635, 1942.
4. Simms, Henry S., Parshley, Mary S., and Pitt, Ruth B.: Fat Deposition in Vitro Caused by Lipfanogens and Opposed by Antilipfanogen. *J. Gerontol., 2:* 205-216, 1947.

FORREST E. KENDALL: *Lipid Metabolism* (Goldwater Memorial Hospital, New York, New York)

Last winter I was asked to summarize the biochemistry of arteriosclerosis, putting down only the facts which could, *with certainty,* be said to be related to the disease. The task was extraordinarily easy. Information was available concerning changes in the composition of arterial walls coincident with the development of arteriosclerotic lesions, but beyond that point certainty did not exist.

It was logical to conclude that since the deposition of cholesterol and cholesterol esters is such a characteristic feature of the arterial lesions, some abnormality in the metabolism of cholesterol was involved in the disease. Since it is likely that the cholesterol in the lesions is carried there by the blood stream, it was reasonable to assume that the level and the state of the cholesterol in the blood is an important factor in the disease. But it should be pointed out that at the present time discussion of the metabolism of cholesterol as part of the biochemistry of arteriosclerosis rests upon logic and a kind of logic wherein neither the major nor the minor premises are established.

Since many of us believe that the unraveling of the mysteries of cholesterol metabolism will furnish a clue leading towards a better understanding of what causes arteriosclerosis and what may be done to prevent or to cure it, the recent advances made in this field are extremely important.

During the last two decades notable progress has been made in the development of specific tools and methods for the study of biologic systems. This past year the application of these tools to the study of cholesterol metabolism has been very fruitful.

Some years ago it was shown by isotope techniques that cholesterol was synthesized in the body from acetate and other 2-carbon molecules and that cholesterol could be converted in the body into bile acids and substances at least sim-

ilar to the steriod hormones. This year Gould (5) has reported that cholesterol marked with radioactive carbon, C^{14}, can be completely oxidized to CO_2 in the body, and he has confirmed the finding of Cook (3) that the feeding of cholesterol leads to the excretion of increased amounts of organic acids. Taylor and Gould (7) also reported that in rats and dogs the addition of cholesterol to the diet greatly reduces the rate at which cholesterol is synthesized from acetate by the liver. This indicates that in normal animals there is a sensitive control mechanism which governs the rate at which cholesterol is built up.

As long as it was believed that cholesterol was metabolically inert and that its ultimate fate was excretion in the feces either as cholesterol or coprosterol, workers in this field were justified in focusing their attention upon the concentration and physical state of the cholesterol in the serum. However, if cholesterol is subject to active metabolic changes in the tissues, the emphasis shifts from the serum to the cells. Changes in the serum levels become a symptom rather than a cause of arteriosclerosis. Actually this shift in viewpoint does not diminish the importance of studies of the serum cholesterol. The establishment of some clinical sign or symptom for the early diagnosis of arteriosclerosis is one of the most urgent needs in this field.

The past year has seen a great increase in our knowledge of how cholesterol is transported in the serum. Working upon pools of normal human plasma, Oncley and his associates at Harvard (6) showed that most of the cholesterol in serum was present in large molecules which contain protein and phospholipid as well as cholesterol and cholesterol esters. These substances could readily be fractionated into two groups which were designated as alpha- and beta-lipoproteins. The alpha-lipoprotein contained about 50 per cent protein and 50 per cent lipid. Cholesterol and phospholipid were present in approximately equimolecular proportions. This alpha-lipoprotein contained about one-fourth of the total serum cholesterol and since solutions of it could be frozen and dried without destroying the molecular aggregates, it probably is the most stable form in which cholesterol exists in serum.

Beta-lipoprotein contained about 25 per cent protein and 75 per cent lipid and was composed of about 2 molecules of cholesterol for each molecule of phospholipid. It could be frozen or dried without destroying the molecules. It was estimated that as much as three-quarters of the total serum cholesterol might be present in this fraction. Neither of these fractions contained neutral fat; therefore it is apparent that they do not give a complete picture of the serum lipids.

Additional information has been obtained by Gofman and his associates (4). Lipid-containing molecules have a lower specific gravity than fat-free protein molecules. The specific gravity of serum albumin or gamma-globulin is greater than 1.30. The specific gravity of alpha-lipoprotein is about 1.18 and that of beta-lipoprotein about 1.03. By adjusting the specific gravity of serum to intermediate values by the addition of salts the lighter molecules can be made to rise to the surface when spun in the ultracentrifuge, while the heavier protein molecules sink to the bottom. Gofman isolated the fraction containing the beta-lipoprotein together with any lighter molecules by centrifuging at a specific gravity of 1.065. By subsequently running this lighter material in the analytic centrifuge the different components can be separated, identified by the rate at which they move in the centrifugal field, and the quantity present estimated.

Under the specific conditions chosen by Gofman the beta-lipoprotein fraction moves with a velocity designated as S_f, 3-8. In addition to this fraction there are others which move more rapidly. Gofman has focused his attention on the material that moves with the velocity S_f, 10-20, because the amount of this fraction present seems to be characteristic of a given individual and is affected but little by food intake. The lighter, more rapidly moving fractions with S_f values up to 75 are increased following a meal containing fat.

Chemical analysis of these fractions shows

that they contain cholesterol, cholesterol esters, phospholipids, and neutral fat with very little protein. The cholesterol content of the S_f, 10-20 fraction is about 30 per cent. In normal individuals between 1 and 5 per cent of the total serum cholesterol may be in this fraction. In certain individuals, particularly those with coronary arteriosclerosis, this percentage may be increased to values as high as from 15 to 20 per cent of the total cholesterol.

It seems to many of us that these substances probably are part of the normal mechanism for moving fats from one part of the body to another. A person with a high level of S_f, 10-20 may not be transporting more lipid in this fraction in the course of a day than one with a low level. His cells may be less able to utilize the fat being transported to them; therefore these fractions tend to pile up in the serum.

Barr at Cornell (1) has been studying the variation in the content of alpha-lipoprotein in normal individuals and in patients with different diseases. He finds that in normal individuals this fraction contains about 30 per cent of the total serum cholesterol. Practically none of the normal people have values lower than 20 per cent. Practically none of his arteriosclerotic patients have values above 20 per cent and some of them are as low as 5 per cent. This difference is indicative of a very profound alteration in metabolism involving proteins as well as sterols and lipids.

Only time will show whether the work discussed here is really part of the biochemistry of arteriosclerosis or not. But I will say that I have never known a year when so much stimulating work in this field has appeared, when so many interesting problems have opened up, or when hope for a final solution of the problem of arteriosclerosis seemed so bright.

References

1. Barr, D.: Personal communication.
2. Bloch, K.: Metabolism of Acetic Acid in Animal Tissues. *Physiol. Rev., 27:* 574-620, 1947.
3. Cook, R. P.: Cholesterol Metabolism. *Biochem. J., 47:* 600-605, 1950.
4. Gofman, J. W., Jones, H. B., Lindgren, F. T., Lyon, T. P., Elliott, H. A., Strisower, B. S.: Blood Lipids and Human Atherosclerosis. *Circulation, 2:* 161-178, 1950.
5. Gould, R. G.: The Comparative Metabolism of Dietary and Endogenous Cholesterol Differentiated by Use of Radioactive Carbon. Abstract. *Circulation, 2:* 467, 1950.
6. Oncley, J. L., Gurd, F. R. N., and Melin, M.: Preparation and Properties of Serum and Plasma Proteins. XXV: Composition and Properties of Human Serum Beta-Lipoprotein. *J. Am. Chem. Soc., 72:* 485-464, 1950.
7. Taylor, C. B., and Gould, R. G.: Effect of Dietary Cholesterol on Rate of Cholesterol Synthesis in the Intact Animal Measured by Means of Radioactive Carbon. Abstract. *Circulation, 2:* 467, 1950.

ALBERT I. LANSING: *Aging of the Arterial Wall* (Department of Anatomy, Washington University School of Medicine, St. Louis, Missouri)

This report summarized data and conclusions reported in a series of papers published in the Journal of Gerontology and the American Journal of Pathology:

Aging and Calcification of the Human Coronary Artery. A. I. Lansing, H. T. Blumenthal, and S. H. Gray, Journal of Gerontology, *3:* 87-97, 1948.

Calcium and Elastin in Human Arteriosclerosis. A. I. Lansing, M. Alex, and T. B. Rosenthal, Journal of Gerontology, *5:* 112-119, 1950.

Significance of Medial Age Changes in the Human Pulmonary Artery. A. I. Lansing, M. Alex, and T. B. Rosenthal, Journal of Gerontology, *5:* 211-215, 1950.

Atheromatosis as a Sequel to Senescent Changes in the Arterial Wall. A. I. Lansing, M. Alex, and T. B. Rosenthal, Journal of Gerontology, *5:* 314-318, 1950.

Calcification of the Media of the Human Aorta and Its Relation to Intimal Arteriosclerosis,

Ageing and Disease. H. T. Blumenthal, A. I. Lansing, and P. A. Wheeler, American Journal of Pathology, *20:* 665-687, 1944.

The Interrelation of Elastic Tissue and Calcium in the Genesis of Arteriosclerosis. H. T. Blumenthal, A. I. Lansing, and S. H. Gray, American Journal of Pathology, *26:* 989-1009, 1950.

Two essential points were made: 1) in the human, intimal lesions are for practical purposes invariably associated with medial changes; the usual pattern of medial damage involves calcification of elastic tissue; and 2) the calcification of medial elastic tissue precedes the formation of intimal plaques.

CHARLES A. WOERNER: *Microscopic Anatomy of the Arterial Wall*

(Department of Anatomy, University of Louisville School of Medicine, Louisville, Kentucky)

THE intima of arteries in young individuals is described as a single layer of endothelial cells lying on a few scattered connective tissue cells and the internal elastic lamina. With age the intima tends to thicken, the endothelium may consist of a number of layers of cells, and the amount of connective tissue in the subendothelial connective tissue increases. Whether lipid is deposited directly into the endothelial cells by pre-existing phagocytes or lipophages is not definitely settled.

Leary (5) and Gordon (1) have presented arguments in favor of the principle that lipid is carried to the lesion in the arterial wall by phagocytic cells that were formerly fixed macrophages as Kupffer cells. On the other hand Kuntz and Sulkin (3) have presented experimental evidence to support the view that lipid is deposited directly into the endothelial cells at the site of the arterial lesion. The endothelial cells then become phagocytic.

Knisely and his associates (2) in their studies of living liver preparations described the transformation of endothelial cells of the liver into "Kupffer cells." They stated that any endothelial cell of the liver sinusoids will phagocytize particles and not only specialized Kupffer cells. Kuntz and Sulkin would extend this principle and consider that any endothelial cell of the arterial wall may phagocytize lipids in the development of atheromatous lesions.

The intima of young arteries contains no capillaries. As the young intima is very thin, only one to three cells in thickness, no special blood supply is required. In older arteries where the intima becomes markedly thickened capillaries grow into it. Winternitz (9) and Wartman (7) have described vasa vasorum in the thickened intima of senile arteries. The relation of the vasa vasorum to the etiology of arteriosclerosis needs further clarification.

While arterial lesions have been described as following atheromatous plaques forming in the endothelium and interfering with the nutrition of the underlying media and thereby causing medial degeneration, changes in arteries leading to the development of arteriosclerosis, and entirely independent of changes in the intima, have been described by Lansing (4), who does not accept the view that atheromatous plaques in the intima are usually primary and the medial changes secondary. The internal elastic lamina separating the intima and media does not seem to protect significantly the media. It tends to split into more than one layer in older arteries.

The vasa vasorum of the media of arteries have been described by Winternitz (9), Wartman (7), and Schlichter (6). I undertook a study of the vasa vasorum of the aorta and coronary arteries in the dog in which investigation the vasa vasorum were demonstrated by the method described by Williams (8). The animal was anaesthetized and the blood washed out with physiologic salt solution. Then a solution of potassium dichromate was injected to fill the smaller arterioles and capillaries. The dichromate was then precipitated by the injection of lead acetate resulting in a finely

divided precipitate of lead chromate. The arteries studied were imbedded in celloidin and sections 400 μ thick were cut.

In the aorta of the dog very few vasa vasorum were found arising from the intimal surface. The ascending aorta was supplied by branches of the coronary arteries, the descending aorta by branches from the intercostal arteries. A few, usually not more than 10 or 12, vasa were found arising from the intimal surface of the aorta at the arch. These small arterioles, 20 to 30 μ in diameter, passed out through the inner two thirds of the aortic media without branching. They almost always soon joined the vasa coming from the adventitia.

In some of these preparations extravasations of the injection mass were found in the outer media. These masses may indicate areas of potential hemorrhage as occur in medial necrosis and in some types of aortic aneurysm. The depth to which the vasa vasorum extended from the adventitia varied. In most areas the capillaries were found only in the outer third of the media; in other areas the capillaries extended throughout much of the middle third. The inner third of the media practically never had any capillaries in it. In a limited number of human aortas (5 specimens) the distribution of the vasa vasorum was very similar to that found in the dog.

The vasa vasorum form an extensive network in the adventitia of the aorta, which is prominent in the junction of the adventitia and media. Another network is seen at the junction of the outer and middle thirds of the media. The inner two thirds of the media is practically avascular in the "normal" aorta. In medium sized muscular arteries, as the iliac and femoral, there seems to be more vasa arising from the intimal surface, as described by Winternitz (9), but in these arteries, as in the aorta, capillaries are rarely if ever found in the inner third of the media.

Summary

While lipid deposition by lipophages migrating to the arterial lesions of arteriosclerosis has been described there is considerable evidence that the lipid deposits directly into the arterial endothelium. In spite of considerable evidence that the intimal lesion is primary, initial changes in the media followed by changes in the intima have been described.

The vasa vasorum with few exceptions arise from branches of the larger arteries and enter the arterial wall from the adventitia. They usually form two networks, one at the junction of the adventitia and media and another between the outer and middle third of the media. Occasionally capillaries extend into the middle third of the media but only very rarely into the inner third. In normal arteries vasa vasorum arising from the intimal surface are rare. The normal intima does not contain capillaries, but capillaries develop in pathologically thickened intima.

References

1. Gordon, I.: Mechanism of Lipophage Deposition in Atherosclerosis. *Arch. Path., 44:* 247-260, 1947.
2. Knisely, M. H., Block, E. H., and Warner, L.: Selective Phagocytosis I. *Det Kongelige Danske Videnskabernes Selkabs Biologiske Skrifter,* Bind IV. Nr. *7:* 1948.
3. Kuntz, A., and Sulkin, N. M.: Lesions Induced in Rabbits by Cholesterol Feedings with Special Reference to Their Origin. *Arch. Path., 47:* 248-260, 1940.
4. Lansing, A. I., Alex, M., and Rosenthal, T. B.: Atheromatosis as a Sequel to Senescent Changes in the Arterial Wall. *J. Gerontol., 5:* 314-318, 1950.
5. Leary, T.: The Genesis of Atherosclerosis. *Arch. Path., 32:* 507-555, 1941.
6. Schlichter, J. C.: Studies on the Vascularization of the Aorta in the Normal Dog. *Am. Heart J., 32:* 770-777, 1946.
7. Wartman, W. B.: Hemorrhage into the Arterial Wall as a Cause of Peripheral Vascular Disease. *Am. Heart J., 39:* 79-87, 1950.
8. Williams, T. W.: The Visualization of Vertebrate Capillary Beds by Intravascular Precipitation of Lead Chromate. *Anat. Rec., 100:* 115-126, 1948.
9. Winternitz, M. D., Thomas, R. M., and LeCompte, P. M.: *The Biology of Arteriosclerosis.* C. C. Thomas, Springfield, Illinois, 1938.

JOHN ESBEN KIRK: *Metabolism of Arteria Tissue* (Division of Gerontology, Washington University School of Medicine, St. Louis, Missouri)

In comparison with the extensive literature dealing with experimental arteriosclerosis the number of investigations pertaining to the normal and abnormal metabolism of arterial tissue is rather small. In spite of this scarcity of data I have thought that it might be of interest to give a summary of the existing publications. Such a review will at least serve to emphasize the need for further research in this field.

As shown by Woerner (14), the internal half or two-thirds of the aortic media may be regarded as a nearly avascularized tissue. This fact can be brought out not only by injection experiments, but also through analyses of the blood content of homogenates, prepared from the media. If such homogenates are analyzed for hemoglobin by the gasometric method of Van Slyke and Neill (13), a zero reading for hemoglobin will be found. For further study of the blood content of the human aortic media From Hansen and I have recently developed a sensitive benzidine method, capable of detecting blood in dilutions up to 1:50000. By means of this technique we have found the blood content of the human aortic media to range between 0.01 to 0.1 per cent. As a consequence of this nearly complete absence of blood from the aortic wall, homogenates of the tissue will appear milk- or cream-colored.

The question of how the luminal one-half or two-thirds of the aortic media receives its oxygen supply and supply of nutrients—from the vasa vasorum, the lumen of the vessel, or from both of these sources—is a very important one, but a question which as yet must be considered as unsolved. An excellent review of this subject, based both on anatomic considerations and on deductions from pathologic findings was published in 1936 by Ramsey (10).

My summary will be limited to a review of the respiratory metabolism of arterial tissue in vitro, to a discussion of enzymes demonstrated in the arterial wall, and to a report on publications dealing with non-steroid lipid synthesis by the surviving arterial tissue.

The first of these subjects, the respiratory metabolism of arterial tissue, has been studied by Lazovskaya (9) in Leningrad in 1943, and by Briggs (2) and his associates at the University of California in 1949. In both of these investigations aortic tissue from rats was used. As will be seen from table 1 the findings in the American and Russian investigations show only partial agreement.

In Lazovskaya's studies from 1943 homogenates of the rat aorta were prepared in phosphate buffer solution and the respiration measured by the direct Warburg technique at ten

RESPIRATION OF RAT AORTIC TISSUE

	Young Rats	Old Rats
Lazovskaya, 1943	Q_{O_2}	Q_{O_2}
Spontaneous respiration, homogenate	2.7	0.2
Addition of succinate, homogenate	4.6	0.6
Addition of succinate and cytochrome c, homogenate	4.0	0.8
Briggs et al., 1949		
Spontaneous respiration, homogenate	0.0	0.0
Spontaneous respiration, tissue slices	1.1	1.1
Addition of succinate, tissue slices	2.6	2.3

minute intervals for one hour, during which period the oxygen uptake was found to remain constant. By this technique a Q_{O_2} value of 2.7 was observed for aortic tissue from young rats about 3 weeks' age. In a group of 1 year old rats the oxygen consumption of the arterial tissue was found to be much lower, about 1/14th of that of the young rats, with a Q_{O_2} value of only 0.2.

Following addition of succinate to the homogenates a notable rise in the respiration was observed, namely an increase from 2.7 to 4.0 in the sample from the young animals, and from 0.2 to 0.6 in the preparations from the old rats. Approximately the same Q_{O_2} values were noted when, besides succinate, cytochrome c was added to the flask content. These latter values give a measure of the capacity of the succinic dehydrogenase system of the tissue. Since after the addition of succinate and cytochrome c the Q_{O_2} values of the aortic tissue from the old rats still were much lower than the oxygen uptake in the homogenates from the young rats, it was concluded by Lazovskaya that a marked decrease in the succinic dehydrogenase capacity takes place with aging of the arterial tissue.

In the studies by Briggs and associates in 1949 on the respiration of rat aortic tissue both the homogenate and the tissue slice techniques were used. As it will be seen from the table, Briggs, in contrast to Lazovskaya, failed to observe a definite oxygen consumption by tissue homogenates, whereas with the use of tissue slices Q_{O_2} values of about 1 were noted. This figure is about one-tenth of that found for rat liver slices. It is possible that the difference between the oxygen uptake of homogenates in Lazovskaya's and in Briggs' experiments is due to differences in the homogenization technique used.

A further discrepancy between the American and the Russian observations on rat aortic tissue is the finding of practically the same Q_{O_2} values for young and old arterial tissue in Briggs' experiments as contrasted to the marked difference between young and old animals noted by Lazovskaya. Both the American and the Russian investigators are, however, in agreement on one point, namely with regard to the effect of succinate addition. As seen from the table such addition also in Briggs' experiments was followed by a marked increase in the Q_{O_2} value. A definite but smaller increase in the oxygen consumption was further noted by Briggs after addition of lactate, pyruvate, alpha-ketoglutarate, citrate, and acetate, whereas glucose, glycine, and alanine were without noticeable effect on the Q_{O_2} values.

This response to succinate, in combination with the observation by Briggs that addition of malonate produced an inhibition of the oxygen uptake, indicate, as did also Lazovskaya's results, that succinic dehydrogenase participates in the metabolic process. Since also fluoride was found to exert an inhibition of the respiration, it may be concluded that phosphorylated intermediates are involved in the metabolism. These results, in addition to the oxidative response to pyruvate and to some members of the tricarboxylic acid cycle, provide evidence that carbohydrate is utilized in the arterial tissue.

In reviewing the interesting findings by Lazovskaya and by Briggs it should, however, be noted that so far no observations have been reported on human arterial tissue and that in the experiments on animal tissue studies on the anaerobic metabolism of the arterial tissue, on the rate of glycolysis, are lacking.

The studies by Briggs and his associates on the oxygen uptake of rat aortic tissue were extended to include measurements on aortic tissue from rats which had been fed thyroid for ten days before the animals were sacrificed and determinations on tissue from another group of animals which had been treated with propylthiouracil for a thirty day period. It is of considerable interest that the aortas from the thyroid treated rats showed a 25 per cent increase in oxygen consumption as compared with the untreated animals, whereas the propylthiouracil treated group showed Q_{O_2} values 20 per cent lower than normal.

Concerning the enzyme systems of the arterial wall the investigations are also rather few. In 1949 Baló, Banga, and Josepovits

(1) in Czechoslovakia demonstrated the presence of a specific ATP-pyrophosphatase with a pH optimum at 9.4 in the human aortic wall, and in the same year Kirk and Prætorius (6, 7, 8) reported the presence in the human aortic media of a monophosphatase, capable of splitting disodium phenylphosphate and disodium p-nitrophenylphosphate. The pH optimum for this phosphatase was found to be 5.7 and it was further observed that the phosphatase could be inhibited by fluoride addition.

Phosphatases with a pH optimum in the range of 5.5 to 6.0 have also been reported present in other tissues. The main interest in the finding of the phosphatase lies in the importance which this observation may have in the general discussion on the mechanism of arterial calcification. Since previous investigators had failed to find a phosphatase in the arterial wall—and these negative results can be explained by the fact that earlier studies had been performed only at an alkaline pH—it has generally been contended that calcification of the arteries could not be brought about by a mechanism analogous to that which is believed to be operating in calcification of bone tissue. Whether the aortic phosphatase has any significance for the calcification of the artery is so far unknown, but the presence of the enzyme in the aortic wall will have to be considered in future discussions on arterial calcification.

In the Division of Gerontology at Washington University From Hansen and I (5) have recently been successful in demonstrating another enzyme, carbonic anhydrase, in the human aortic media. We were led to investigate for the presence of this enzyme through reports in the literature on the occurrence of carbonic anhydrase in two other avascularized tissues, namely the cornea and the lens.

Experiments were conducted employing two techniques: 1) the procedures of Brinkman, Margaria, and Roughton (3) for determination of the dehydration of carbonic acid, and (2) the colorimetric procedure of Trethewie and Day (12) for measuring the rate of hydration of carbon dioxide. By both these methods the carbonic anhydrase activity in the aortic media observed was considerably higher than that which could be accounted for by the traces of blood present in the tissue. In all the experiments both the concentration of blood in the aortic media samples and the carbonic anhydrase activity of the blood from the same individual were determined and the enzyme values for the media corrected for the traces of blood present. It could be calculated that the carbonic anydrase activity of the arterial tissue was about 1/200 to 1/600 of that of a similar weight of red blood cells. As would have been expected the carbonic anhydrase in the aortic media was found to be inhibited by addition of sulphonamide.

It is perhaps too early to discuss the eventual significance of carbonic anhydrase in the human aortic wall. It might, however, be mentioned that just as it is conceivably difficult for the avascularized tissue to obtain the necessary supply of oxygen and nutrients because of the long diffusion way, it is probably equally difficult for these tissues to get rid of the metabolic end product, carbon dioxide. The function of carbonic anhydrase in the arterial wall may be the facilitation of the removal of carbonic acid through its conversion to the more easily diffusible carbon dioxide gas. When data have been provided concerning the rate of aerobic and anaerobic metabolism in the human aorta it may prove possible to define the function of the enzyme more clearly.

The only publication on the ability of arterial tissue to synthesize lipids is one by Chernick and his associates (4) from the University of California in 1949. In these important investigations both the synthesis of fatty acids and the synthesis of phospholipids were studied.

For the study of the fatty acid synthesis C 14 labelled acetate was added to slices of rat aorta placed in bicarbonate-Ringer solution. After three hours the fatty acids were extracted and their content of C 14 determined. It was found that in the three hour period 0.4 to 0.7 per cent of the labelled acetate had been converted to fatty acids, so that a synthesis of

fatty acids from this 2-carbon compound had been proved.

Similar experiments using inorganic phosphate labelled with P 32 showed an incorporation of about 0.8 per cent of the added phosphate into phospholipids per gram of arterial tissue in the course of two hours. This figure is quite appreciable when it is considered that the phospholipid synthesis by rat liver slices under the same conditions amounts to about 5 per cent per gram of tissue, or a synthesis which is only about 6 times higher.

Although the experimental data on the metabolism of arterial tissue reported here are somewhat few and scattered, the observations by Briggs on the effect of thyroid and propylthiouracil on the oxygen uptake of rat aortic tissue and the findings by Chernick of an ability of the rat aorta to synthesize both fatty acids and phospholipids suggest that a further knowledge of the normal and abnormal arterial tissue metabolism might contribute to the understanding of the factors responsible for the development of arteriosclerosis. The recent finding by Rinehart and Greenberg (11) of production of arteriosclerosis in pyridoxine deficient monkeys would also seem to emphasize this point of view.

It is my belief that metabolism studies performed on fresh human arterial tissue obtained at autopsy likewise might contribute findings of value. Such studies, including investigations on the respiration and the rate of glycolysis of the human aortic media and measurements of the diffusion coefficients of gases, nutrients, and electrolytes for this tissue are at present in progress at the Division of Gerontology, Washington University, St. Louis.

References

1. Baló, J., Banga, I., and Josepovits, G.: Enzymic Activity of the Aorta. Adenylpyrophosphatase of the Aorta. *Ztschr. f. Vitamin-, Hormon-, und Fermentforschung, 2:* 1-10, 1949.
2. Briggs, F. N., Chernick, S., and Chaikoff, I. L.: The Metabolism of Arterial Tissue. I. Respiration of Rat Thoracic Aorta. *J. Biol. Chem., 179:* 103-118, 1949.
3. Brinkman, R., Margaria, R., and Roughton, F. W. J.: The Kinetics of the Carbon Dioxide-Carbonic Acid Reaction. *Philosoph. Transact. Royal Soc. London, Ser. A, 232:* 65-97, 1933-1934.
4. Chernick, S., Srere, P. A., and Chaikoff, I. L.: The Metabolism of Arterial Tissue. II. Lipid Synthesis, the Formation in Vitro of Fatty Acids and Phospholipides by Rat Artery with C_{14} and P_{32} as Indicators. *J. Biol. Chem., 179:* 113-118, 1949.
5. Kirk, J. E., and From Hansen, P.: The Presence of Carbonic Anhydrase in the Media of the Human Aorta. *J. Lab. & Clin. Med., 36:* 844-845, 1950.
6. Kirk, E., and Prætorius, E.: The Presence of a Phosphatase in the Human Aortic Wall. *J. Lab. & Clin. Med., 34:* 1617-1618, 1949.
7. Kirk, E., and Prætorius, E.: Presence of a Phosphatase in the Human Aortic Wall. *Science, 111:* 334, 1950.
8. Kirk, J. E., and Prætorius, E.: Further Studies on the Human Aortic Phosphatase. *Circulation, 2:* 477-478, 1950.
9. Lazovskaya, L. N.: The Change in Respiration of Blood Vessels with Age. *Biochimia, 8:* 171-176, 1943.
10. Ramsey, E. M.: Studies in the Pathology of Vascular Disease: Nutrition of the Blood Vessel Wall. *Yale J. Biol. & Med., 9:* 14-36, 1936-37.
11. Rinehart, J. F., and Greenberg, L. D.: Arteriosclerotic Lesions in Pyridoxine Deficient Monkeys. *Fed. Proc., 7:* 278, 1948.
12. Trethewie, E. R., and Day, A. J.: Some Observations on the Secretion of Acid. *Austral. J. of Exper. Biol. & Med. Science, 27:* 429-440, 1949.
13. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement. *J. Biol. Chem., 61:* 523-573, 1924.
14. Woerner, C. A.: Microscopic Anatomy of the Arterial Wall. *J. Gerontol., 6:* 165-166, 1951.

CURRENT COMMENT

Division of Maturity and Old Age

The Division on Maturity and Old Age of the American Psychological Association invites the affiliation of members of the Gerontological Society. The Division on Maturity and Old Age was organized: (1) to further the study of psychologic development and change through the adult years and old age, (2) to discover and foster the use of means for dealing with such changes, (3) to collaborate with other groups or organizations in these problems, and (4) to disseminate knowledge of these matters. Membership is open to nonpsychologists who are interested in the work of the Division. There are now over 200 members, including individuals from such fields as medicine, social service administration, and industrial personnel administration.

The division sponsors an annual program of symposia and scientific papers on the psychologic aspects of aging. Abstracts of these papers are published in the American Psychologist, which is sent to all members together with the Newsletter of the Division and the Directory of the members of the American Psychological Association. Dues for affiliate members is $4.00 per year, which includes these publications.

Information and application blanks may be secured from the Chairman of the Membership Committee, Dr. James E. Birren, Committee on Mathematical Biology, University of Chicago, Chicago 37, Illinois.

Committee on Aging and Geriatrics

A Committee on Aging and Geriatrics has been established in the Federal Security Agency under the Chairmanship of Mr. Clark Tibbitts. Mr. Tibbitts, Assistant Chief of the Division of Public Health Methods, Public Health Service, served as Director of the National Conference on Aging called by the Federal Security Administration in Washington last summer. The Committee is the result of the President's letter of last June requesting the Federal Security Agency to explore with all appropriate groups within and outside the Federal Government the problems arising from the increasing proportion of older persons in our population.

The Committee on Aging and Geriatrics, working with private organizations and Government agencies, will have three major purposes: (1) to develop methods for the integration of older persons into our total mobilization efforts, (2) to continue the collection of information about the characteristics and potentialities of older people about the problems experienced by them and their families and about programs that are being developed to meet these problems, and (3) to satisfy the

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The hieroglyphics, "The Beginning of the Book for Transforming an Old Man into a Youth," at the top of this editorial page, are from the Edwin Smith Surgical Papyrus, translated by Professor John Breasted, University of Chicago Press.

increasing demands since the National Conference on Aging for information and guidance to public and private organizations interested in fitting older people into active participation in normal family, social, and community activities.

Study of Retirement

The Lilly Endowment, Inc. of Indianapolis has recently awarded the Cornell Social Science Research Center a grant to conduct a seven year longitudinal study of the impact of occupational retirement in the United States on physical and mental morbidity and mortality. The study will be based on a sample of the labor force 64 years of age. The subject will be observed until their seventieth birthday, and comparisons will be made of those who retire with those who do not and those whose retirement is arbitrary and unplanned with those whose retirement is voluntary and planned. A principal aim of the study is to check systematically on the validity of the hypothesis that there are significant differentials in illness and mortality incidence between those who retire and those who continue in gainful employment.

Study of Performance Level with Aging

W. A. Owens, Head of the Department of Psychology of Iowa State College of Agriculture and Mechanic Arts, has reported on an interesting study made under his direction. The purpose of the study was to investigate the effects of a 30 year age increment upon performance level in 8 mental functions. One of the results of the study was the observation that there were no significant decreases in mean test score accompanying the 30 year age increment since the original testing. Highly significant increases in performance on 4 of the tests as well as in the mean total score imply that the component members of a population originally possessing college level ability would in general be more intellectually able at 50 years of age than at 20, athough such a generalization would not hold true for groups of average or inferior mental ability.

News and Notes

The University of Chicago has received a grant from the Rockefeller Foundation for a study of the psychologic meaning of work and retirement. Eugene A. Friedmann is working on the project, which is supervised by Dr. E. W. Burgess, Dr. R. J. Havighurst, and Dr. E. Shanas.

A project in preventive hygiene for later maturity will be supported by the U. S. Public Health Service in Chicago under the direction of Dr. J. Weinberg and Dr. R. J. Havighurst. Two courses will be given on an experimental basis for people 55 to 65 years old. One course will meet once a week for thirty weeks and the other will be a full time one month program in the summer. Content of the course will consist of medical and psychologic examinations; lectures and consultations on health, nutrition, financial management, housing, family problems, spiritual development and philosophy of life; and recreational activities

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A conference dealing with Problems of an Aging Population will be held on the Northwestern University campus June 7 and 8. Topics will include discussions of the problems of aging in the United States, social implications of an aging population, our aging labor force, and anticipating age with assurance.

Dr. Sidney L. Pressey has received a special grant of funds from the Ohio State University providing two fellowships for study of the relationship of employment and age.

A course of lectures and discussions arranged under the sponsorship of a number of the public and private agencies in Montgomery County, Maryland, was held February 2 and 3 at the National Institutes of Health,

Bethesda. The topics covered included the following: Public Health and Aging by Dr. J. M. Mountin, Assistant Surgeon General, U. S. Public Health Service; The Medical Aspects of Aging by Edward J. Stieglitz, Washington, D. C; A Family's Adjustment to Its Aging Members by Mrs. Lindon S. Dodson, Supervisor of Old Age Assistance, Montgomery County Board of Public Welfare; Economic Values in Industrial Aspects by Dr. Ewan Clague of the U. S. Department of Labor; and a discussion on What Should Be Done by Dr. Clark Tibbitts of the U. S. Public Health Service.

A national Conference on Chronic Disease: Preventive Aspects, was held in Chicago, March 12-14, 1950. The National Health Council and the U. S. Public Health Service were co-sponsors.

Dr. Mark Anton Bruck conducted a series of four meetings, November 9, 16, 30, and December 7, on the Psychological Aspects of Advancing Age at the North Hollywood Adult Education Center, Hollywood, California.

Teachers' College, Columbia University, announces a grant of $24,000 for a two-year period by the Carnegie Corporation for a study of the psychology of aging and retirement. The funds will be administered by the Institute of Psychological Research under the direction of Dr. Irving Lorge.

A series of four lectures on aging and retirement were held February 21 to March 21 by the Graduate School, U. S. Department of Agriculture, Washington, D. C. Dr. Edward J. Stieglitz, Mr. Ewan Clague, and Miss Ollie A. Randall were among the speakers.

The Cleveland Conference on Making the Later Years Productive was held January 12, 1951. The keynote address, given by Dr. Edward J. Stieglitz, was followed by a panel discussion. Dr. Anton J. Carlson presented the luncheon address, and in the afternoon there were five round table section meetings, Education and the Longer Life, The Older Worker in the Cold War, Living Arrangements, The Older Person in the Changing Family, and Mental Hygiene.

The Proceedings of the First International Gerontological Congress, under the presidency of Professor L. Brull, have been published in the *Revue Médicale de Liège* (vol. 5, no. 20, pages 593-734). The Proceedings include many of the papers presented at Liège, each paper published in French or English, and the actions taken at the Conference which have led to the development of the Second International Gerontological Congress to be held in St. Louis this September. A complete list of names and addresses of gerontologists in several countries is also included. Those who wish copies may obtain them at $2.50 each from the Journal of Gerontology.

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Disbursements:			
Transferred to Journal Account	4,002.48		
Third Scientific Meeting (St. Louis)	506.89		
Printing and Stationery	202.58		
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Total Disbursements		4,818.08	
Excess of Receipts			570.55
Balance December 31, 1950			$ 844.90

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Balance January 1, 1950		$10,382.46	
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Adjusted Balance January 1, 1950			$11,700.80
Receipts:			
Subscriptions	$ 10,373.15		
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Printing and Mailing Journal	6,212.80		
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Stationery and Printing	380.43		
Shipping and Postage	291.28		
C. C. Thomas for 1946 Back Issues	216.24		
Office Suplies	67.46		
Refunds	43.28		
Typewriter Rental	35.00		
Accounting Service	35.00		
Copyrights	16.00		
Telephone and Telegrams	13.99		
Miscellaneous	8.36		
Total Disbursements		12,286.32	
Excess of Receipts			612.66
Balance December 31, 1950			12,313.46
Recapitulation:			
Cash in Bank			12,263.46
Petty Cash on Hand			50.00
			$12,313.46

(a) The Editorial Account, used in previous years, was closed and the balance transferred to the Journal Account as of January 1, 1950.

(b) Total Salaries for the Year			$3,900.00
Plus: City Income Tax withheld but not remitted until this period		$4.36	
Less: 3% Collection Fee		.30	4.06
			$ 3,904.06

1950 ANNUAL REPORT OF THE MEMBERS OF THE GERONTOLOGICAL SOCIETY, INC., PURSUANT TO SECTION 46 OF THE MEMBERSHIP CORPORATIONS LAW OF NEW YORK

TO THE MEMBERS OF THE GERONTOLOGICAL SOCIETY, INC.:

The members of the corporation submit the following report for the year ended December 31, 1950.

(1) Real property		$ 0.00	$ 0.00
Personal property:			
Cash deposit in the First National Bank: Membership Account		844.90	
Cash deposit in Boatmen's National Bank: Journal Account		12,263.46	
Petty cash fund		50.00	
Office furniture (St. Louis)		100.00	
Estimated value, back issues of the Journal of Gerontology, 1947, 1948, 1949, and 1950 (St. Louis)		6,400.00	
Total			19,658.36
(2) Receipts: The amount and nature acquired during the year ended December 31, 1950:			
Membership dues		1,026.15	
Subscriptions to Journal of Gerontology		10,373.15	
Advertising, reprints, excess engraving and tabular matter in Journal of Gerontology		2,525.83	
Total			13,925.13
(3) Disbursements: The amount applied, appropriated or expended during the year ended December 31, 1950:			
Printing and mailing Journal		6,212.80	
Salaries		3,904.05	
Publicity and travel		623.09	
Reprints		439.33	
Stationery and printing		583.01	
Shipping and postage		394.76	
C. C. Thomas for 1946 back issues		216.24	
Office supplies		70.11	
Refunds		43.28	
Typewriter rental		35.00	
Accounting service		35.00	
Copyrights		16.00	
Telephone and telegrams		13.99	
Miscellaneous		8.36	
Third Scientific Meeting		146.89	
Total			12,741.92
(4) Summary:			
Cash balance on hand January 1, 1950		11,975.15	
Receipts during year ended Dec. 31, 1950		13,925.13	
Disbursements during such year		12,741.92	
Leaving a balance of			$13,158.36

(5) The names and places of residence of the persons who have been admitted to membership in the corporation during the year ended December 31, 1950:

Dr. Warren Andrew
Department of Anatomy
George Washington University
School of Medicine
1335 H St., N.W.
Washington 5, D. C.

Dr. Edward L. Bortz
2021 West Girard Avenue
Philadelphia, Pennsylvania

Dr. George E. Wakerlin
Department of Physiology
University of Illinois
College of Medicine
1853 West Polk St.
Chicago 12, Illinois

Dr. Oscar Kaplan
Department of Psychology
San Diego State College
San Diego, California

Dated January 31, 1950
State of Missouri } ss.
City of St. Louis }

C. J. Van Slyke and John Esben Kirk, being severally duly sworn, each for himself says: That the said C. J. Van Slyke was President, and that the said John Esben Kirk was Treasurer of the Gerontological Society, Inc. for the year 1950; that the foregoing is a report thereof showing the whole amount of personal property owned by said corporation, where located, and where and how invested; the amount and nature of the property acquired during the year ended December 31, 1950, being the year immediately preceding such date, and the purpose, objects, or for which such applications, appropriations, or expenditures have been made; the names of the persons admitted to membership in the corporation during the year; and that the corporation owns no real property; which report is in all respects true to the best of deponents' knowledge and belief.

C. J. Van Slyke, *President*
John Esben Kirk, *Treasurer*

For the benefit of foreign participants in the Second International Gerontological Congress who may wish to visit universities during their stay in America, attention is called to the book, *Trends in Gerontology*, by Nathan W. Shock (Stanford University Press, 1951, $2.50) in which a survey is given of American research in institutions conducting investigations in the field of gerontology.

A list of university sponsored research work in gerontology in the United States and Canada is also available. The list, which is based on a questionnaire sent out in July, 1950, to the departments of anatomy, biology and biochemistry, physiology, pathology, medicine, and zoology of 333 American and 53 Canadian universities from which a total of 175 replies were received, may be obtained by writing to the Journal of Gerontology, Scott and Euclid, St. Louis 10, Missouri.

Gerontological Society, Inc. Committee Members for 1951

Membership Committee:

Nathan W. Shock, Chairman
Gerontology Section, U.S.P.H.S.
Baltimore City Hospitals
Baltimore 24, Maryland

Albert I. Lansing
Department of Anatomy
Washington University School of Medicine
St. Louis 10, Missouri

Oscar J. Kaplan
Department of Psychology
San Diego State College
San Diego, California

William B. Kountz
Division of Gerontology
Washington University School of Medicine
St. Louis 10, Missouri

Ollie A. Randall
Community Service Society
105 East 22 Street
New York 10, New York

Program Committee:

John Esben Kirk, Chairman
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Washington University School of Medicine
St. Louis 10, Missouri

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Committee on Human Development
University of Chicago
Chicago 37, Illinois

Oscar J. Kaplan
Department of Psychology
San Diego State College
San Diego, California

O. J. Pollak
Quincy City Hospitals
Quincy 69, Massachusetts

Margaret Chieffi
Division of Gerontology
Washington University School of Medicine
St. Louis 10,. Missouri

E. T. Engle
630 West 168 Street
New York 32, New York

Nominations Committee:

C. J. Van Slyke, Chairman
National Heart Institute
National Institutes of Health
Bethesda 14, Maryland

Clive M. McCay
Stocking Hall
Cornell University
Ithaca, New York

Joseph Aub
Massachusetts General Hospital
Fruit Street
Boston 14, Massachusetts

Constitution and By-Laws Committee:

Warren Andrew, Chairman
Department of Anatomy
George Washington University School of Medicine
Washington 5, D. C.

Constitution and By-Laws Committee: (Continued)

Robert J. Havighurst
Committee on Human Development
University of Chicago
Chicago 37, Illinois

F. L. Hisaw
Department of Biology
Harvard University
Cambridge, Massachusetts

Jean Oliver
Long Island College of Medicine
335 Henry Street
Brooklyn, New York

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National Institutes of Health
Bethesda 14, Maryland

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Department of Legal Medicine
Harvard University School of Medicine
Boston 15, Massachusetts

Albert I. Lansing
Department of Anatomy
Washington University School of Medicine
St. Louis 10, Missouri

Affiliation Committee:

Henry A. Schroeder, Chairman
Department of Internal Medicine
Washington University School of Medicine
St. Louis 10, Missouri

E. Cowles Andrus
24 East Eager Street
Baltimore 1, Maryland

Irvine H. Page
Cleveland Clinic
Euclid at East 93 Street
Cleveland 6, Ohio

Willard O. Thompson
700 North Michigan
Chicago 11, Illinois

Public Foundation Committee:

Chauncey D. Leake, Chairman
University of Texas School of Medicine
Galveston, Texas

Oliver H. Lowry
Department of Pharmacology
Washington University School of Medicine
St. Louis 10, Missouri

Joseph Aub
Massachusetts General Hospital
Fruit Street
Boston 14, Massachusetts

Henry S. Simms
Department of Pathology
College of Physicians and Surgeons
New York 32, New York

William deB. Mac Nider
University of North Carolina
Chapel Hill, North Carolina

William H. Stead
Federal Reserve Bank of St. Louis
St. Louis, Missouri

Thomas C. Desmond
94 Broadway
Newburgh, New York

BOOK REVIEWS

WORK LIFE EXPECTANCY

TABLES OF WORKING LIFE. LENGTH OF WORKING LIFE FOR MEN, Bulletin No. 1001, U. S. Department of Labor, Bureau of Labor Statistics, August, 1950, 74 pages, paper bound, offset printed, for sale by the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C., 40¢.

The current state of international affairs tends to obscure, for the moment, some of the domestic economic and social problems of the nation. And yet, in many instances, there is a direct relationship between the successful implementation of international commitments and the effective solution of domestic problems. In each category, the extent of our knowledge of basic facts that relate to the immediate problems confronting us is a major factor in determining the kind of policy decisions that are made.

A number of domestic problems arise from the long-observed tendency for the average work life of workers to decline at the same time that their life expectancy has tended to lengthen. But unfortunately, not much in the way of factual material that would contribute to a full understanding of the scope of these problems has been developed. Because it helps fill this gap in our knowledge, this publication of the Bureau of Labor Statistics is significant.

The Tables of Working Life, Length of Working Life of Men, is the first of a series of studies of the length and pattern of the working life of men and women in the United States. It contains detailed tables on the work life expectancy of men as well as brief descriptions of the patterns of working life, differentials by color and residence, and the application of the tables to analyses of problems of old-age dependency, labor force problems, and occupational outlook.

The method used by the Bureau in constructing the tables of working life for men is similar to that used in setting up a standard life table. In each, the experiences of a given number of persons assumed to be born at the same time are followed through successive years. The work life expectancy tables thus show what might be expected for men of a given age if the prevailing rates of mortality and of labor force participation should remain unchanged over their life span.

Earlier in our history, the average life expectancy and the average working life expectancy for men were almost identical. But with changing economic and social conditions, differences between the two began to develop. Today, workers on the average can look forward to living several years beyond the number of years of labor force participation. This, of course, has many implications with respect to the whole complex of problems involving our people in the upper age brackets.

Although the principal tables developed in this study are based on conditions that prevailed in 1940, supplementary tables based on 1947 experience also are included in the study. In view of the probability that international commitments will result in a tight labor market for some years to come, the abridged 1947 tables may prove more valuable to analysts than the tables based on conditions that existed a decade ago.

The report points out that the work life tables, like standard life tables, are not forecasts of future trends. Later in the study, however, the 1940 and 1947 data are related to estimates shown for 1900 to project two possible trends into the next quarter century. One is based on the assumption that 1940 labor force participation rates for young workers continue and that the proportion of workers over 55 years of age continues to decline. The second assumes that 1947 rates of labor force participation will be maintained. Each assumes a continued favorable trend in mortality rates.

Under the first alternative the increase in

life expectancy would be reflected in a longer period of retirement from the labor force—ten years by 1975 as compared with five years in 1947 for a 20 year old man. At age 60, under these conditions, the average worker could expect to live seventeen more years, but could anticipate working less than half of that time.

These projected trends contrast rather sharply with those that might result if the relatively tight labor market conditions in 1947 prevail. Employment opportunities for the young and old workers were more plentiful in 1947 than in 1940. If these conditions prevailed in 1975, the longer life expectancy at that time would be reflected principally in a longer work life expectancy.

Whether the 1940 or the 1947 tables prove to be most valid for future projections, the fact remains that the availability of this material will be of great value in the analysis of labor market and other problems that confront us.

W. H. STEAD

ASPECTS OF ARTERIOSCLEROSIS

SELECTED STUDIES ON ARTERIOSCLEROSIS, Rudolf Altschul, Charles C Thomas, Publisher, Springfield, Illinois, 1950, 182 pages, $5.50.

As the title of the book clearly states, this is no more than a restricted and highly selected presentation; it is a disappointment to the reader because of the selection. At least in the area of gerontology there is probably no more acute problem than that of arteriosclerosis. Experimental explorations of this problem are at a high water mark. Blood chemistry, lipo-protein studies, chemical studies of arterial lesions, and experimental production of atheroma are all being thoroughly analyzed today. As a consequence, we all are anxious to see synthesis of existing data along the lines of the classical volume by Cowdry.

A book now dealing only with selected studies—selected studies from the author's work—is disappointing. The style of writing is difficult. I find it hard work to rationalize the sequence used in the presentation of the various experiments.

However, all is not bad in Altschul's treatise. His discussion of the cytology of the endothelium is concise but informative and the illustrations are very well done. The classification of terminology is commendable and might be more widely applied. Quite properly, vascular lesions as a consequence of cholesterol administration to animals are referred to as experimental cholesterol arteriosclerosis, lipoidosis as foam cell aggregates, and cholesterolosis as the composite with or without calcification.

Critical evaluation of the various experiments described by Altschul, which included experimental ligature of arteries and cholesterol administration, are left to the reader. In the main it would have been much more worth while had there been an attempt to synthesize the various approaches to the study of arteriosclerosis.

A. I. LANSING

GERMAN GERONTOLOGIC TEXTBOOK

ALTERN UND KRANKHEIT, Max Bürger, Georg Thieme, Leipzig, 1947, 143 pages, 38 R.M.

This monograph by Max Bürger, chief of the Medical University Clinic in Leipzig, represents a valuable contribution to the gerontologic literature. This value is enhanced by the inclusion in the text of 170 illustrations and 163 tables, many of which have not previously appeared in the textbooks on gerontology. The volume contains two main sections, the first dealing with the general physiology and pathology of aging and the second with the clinical features characteristic of diseases in the aged.

The major importance of Bürger's book lies,

in the opinion of the reviewer, in the opportunity which this monograph provides for access to the rather extensive but not widely known German literature in this field. The book can by no means be characterized as a complete or balanced exposition of theoretic and clinical gerontology, but the various chapters are well written and homogeneous. The lack of balance is evidenced particularly in the marked preponderance of consideration given to German investigations. This fact, however, instead of being a disadvantage, would seem to add to the value of the publication for those readers who already are familiar with the standard reference books in this field, such as Cowdry's textbook, since it is exactly the German and Central European contributions which have not been too easily accessible.

Out of the 813 literature references listed as foot-notes in Bürger's book, 716, or 88.2 per cent, represent papers in German journals, monographs, or theses, whereas the remaining references are distributed as follows: American, 43 (5.2 per cent); French, 18 (2.2 per cent); Scandinavian, 13 (1.6 per cent); British, 10 (1.2 per cent); Italian, 4 (0.5 per cent); Argentine, 3 (0.4 per cent); Russian, 2 (0.3 per cent); and Swiss, Belgian, Hungarian, and Chinese each 1 (0.1 per cent).

Although many of the statements in Bürger's book express opinions held by him and his coworkers, which are not substantiated in the presentation, the majority of the statements are either based on data quoted or given in the text or refer to publications to which reference in the literature is given.

The description of the clinical features of the diseases as occurring in old individuals is incomplete, but the chapters contain many isolated interesting observations and comments. The paragraphs on therapeutics seem to the reviewer to be the least interesting feature of the book.

In spite of some criticism of this monograph, the important fact remains that the book contains a large body of valuable data derived from journals usually not covered completely by American textbooks, many of which would seem to be of decisive importance. As an example, a curve on page 337 gives the incidence of hypertrophic arthritis of the spine in various age groups as actually observed in autopsies on 4253 successive cases, and the charts on page 340 show the frequency of this type of arthritis in the shoulder, elbow, knee, and hip joints as found in 1000 postmortem studies.

A similar interest is attached to many of the tables and illustrations in the histologic and anatomic sections which give values for tissue dimensions, analyses of tissue composition, and the results of function tests, data either not included in the more generally used textbooks in this field or which supplement in a valuable manner observations derived in American and British laboratories and institutions.

The slightly different approach to the problems, as evidenced from investigational plans and from the conclusions drawn from observed data, makes several sections of the book quite stimulating reading. Although the book in the reviewer's opinion does not reach the standard of the better American textbooks, Bürger's book raises the question of whether it might not be advantageous to encourage other foreigners to compose a similar comprehensive review of the gerontologic literature of their respective countries. Such reviews would undoubtedly uncover a volume of valuable data at the present accessible only in the native languages and not replaceable merely by lists of literature references from such countries.

There are several misprints in the book, especially in the references to non-German literature, and also some editorial errors (for instance, the description in the legend to figure 144 of the colors shown by the various tissue components in the histophotograph, in spite of the fact that the figure is presented in black and white), but on the whole the presentation is correct and the tables and illustrations easily understandable.

As an introduction to German contributions in the field of gerontology the book can be recommended.

J. E. Kirk

CONFERENCE STUDIES ON AGING

PLANNING THE OLDER YEARS, edited by Wilma Donahue and Clark Tibbetts, University of Michigan Press, Ann Arbor, 1950, 248 pages, $2.50.

This book, a companion volume to *Living in the Later Years,* does its bit—a good bit—to correct the inattention to the advancing years; and it is especially valuable in showing the community's responsibility to plan for the old age of its members. Of this many sided social problem, facet after facet fronts on an area where the individual can do little alone, and where only public policy can and should control. Housing and employment come first to mind as illustrations.

This point of view, which is implicit in most of the studies, is a hearty rebuttal to a few writers and speakers who would solve the problem by leaving it to each individual and, in general, invoke the social and economic values of a period when only 3 per cent, instead of 8 per cent, of the population actually reached what we now consider old age—the 65-and-over bench mark. The thesis is by no means uniform in this collection, but it is supported variously by Ollie A. Randall (talking of living arrangements); Coleman Woodbury (on current housing developments); Henry S. Curtis (on almshouses, poorhouses, and infirmaries); Robert J. Havighurst (on public attitudes toward various activities); Ewan Clague (on social and economic problems of employment); and Harry Becker's piece on labor's stake in employment and retirement.

In one way or another there is a refreshing emphasis on the kind of atmosphere that helps a happy old age. The need of aged people to work constructively, to be wanted, to be effective, and so on, is implicit throughout the warm tone of the work. These studies are not the kind that leaves old age a well-analyzed but desiccated husk. Old age in these essays is a lively, livable period, with a bright eye on the future. At the same time, the reader is spared the sentimental approach of "Come, grow old along with me—"

Most of these essays could be read with profit by community planners, by the clergy, the more realistic law makers, altogether too many social workers, and perhaps even some physicians. Although no volume of this nature can contain everything—and, after all, a good deal that is omitted is contained in its companion volume—a reader misses a more specific and frank approach to health and medical care. There is very little exactly and explicitly to the point, particularly when one remembers the responsibility that seems to be placed on the community as a whole in problems of aging. The index, usually a fair inventory to correct a reader's bias, shows one paragraph on health (as "health security") and two pages on "diseases of old age, research on"—but the index goes farther in other headings, since in another place there is a paragraph on the extraordinarily valuable and productive research in gerontology carried on at Washington University. In extenuation of this minimum attention, it is possible that many of the social aspects dealt with in this book do have a bearing on the health of the aged person.

An error that appears in the introduction by the editors should not be taken to represent the level of editing care and accuracy. On Page 4 the editors say ". . . in this year of 1950, twenty-one million Americans will be sixty-five years of age and over . . ." On page 193 Ewan Clague puts this population figure close to the year 2000—"By the year 2000, we can expect that about twenty-one and one-half million persons [will be 65 or over]." Mr. Clague is the more careful and reliable in his source, and his version is to be preferred.

LOUIS TOWLEY

REPORT ON A CONFERENCE

LIVING THE LATER YEARS, Proceedings of a Conference on Old Age. Marshall College and the Civic Organizations of Huntington, West Virginia, June 20-21, 1950, 162 pages, paperbound.

This volume adds another book to the rapidly growing library of reports on conferences on aging. It is difficult in such conferences to give equal emphasis to all aspects of aging. For its part, the Marshall College conference seems to have stressed the social and economic, rather than the physical, aspects of old age.

Those who do not have access to the presently out-of-print materials published by the New York State Legislative Committee on Problems of Aging will find Walter S. Corrie's summary of these reports very helpful. Several of the other papers particularly those by Clark Tibbitts, R. Clyde White, and Dr. Theodore G. Klumpp should be useful supplementary materials in adult education programs on aging.

E. SHANAS

BOOKS RECEIVED

Books received since December 1, 1950, are acknowledged in the following list. In so far as space and time permit, some will be selected for review in a later issue, but it is unlikely that all will be reviewed.

Altern und Krankheit, by Max Bürger, Georg Thieme, Leipzig, 1947, 413 pages, 38 RM. Reviewed in this issue, page 180.

Burden of Diseases in the U. S., by Alfred E. Cohn and Claire Lingg, Oxford University Press, New York, 1950, 129 pages, 5 separate color charts, $10.00.

Living the Later Years, Proceedings of a Conference on Old Age, Marshall College and the Civic Organization of Huntington, West Virginia, June 20-21, 1950, 162 pages, offset printed.

Memo to Mature Workers re: How to Get a Job, published by the New York State Joint Legislative Committee on Problems of the Aging, 16 page pamphlet, single copies free.

Resources of Old-Age and Survivors Insurance Beneficiaries in Philadelphia and Baltimore, 1949, Federal Security Agency, Social Security Administration, Bureau of Old-Age and Survivors Insurance, Division of Program Analysis, May, 1950, 33 pages, photo offset printed, paper bound.

Social and Biological Challenge of Our Aging Population, Proceedings of the Eastern States Health Education Conference, March 31-April 1, 1949, Columbia University Press, New York, 1950, 183 pages, $2.75.

Surveying Community Needs and Resources for Care of the Chronically Ill, The Institute of Medicine of Chicago, The Central Service for the Chronically Ill, 343 South Dearborn Street, Chicago 4, 1950, 25 page pamphlet, 40¢.

Tables of Working Life. Length of Working Life for Men, Bulletin No. 1001, U. S. Department of Labor, Bureau of Labor Statistics, August, 1950, 74 pages, paper bound, offset printed, for sale by the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C., 40¢. Reviewed in this issue, page 179.

Terminal Care for Cancer Patients, A Study of the Facilities and Services Available and Needed for the Terminal Care of Cancer Patients, The Institute of Medicine of Chicago, The Central Service for the Chronically Ill, 343 South Dearborn Street, Chicago 4, 1950, 211 pages, paper bound, $1.25.

INDEX TO CURRENT PERIODICAL LITERATURE

NATHAN W. SHOCK
Gerontology Section
National Heart Institute
National Institutes of Health

The subject categories are those in *A Classified Bibliography of Gerontology and Geriatrics* by Nathan W. Shock to be published by Stanford University Press, Stanford, California. Only major headings will be used and the Roman numerals correspond to those given in the bibliography. In so far as possible, references are classified according to organ systems. Thus most of the material on Geriatrics will be found under the organ system involved in the disease. Cross references are indicated by number at the end of each section. When available abstract references are given *(B.A.* indicates *Biological Abstracts; P.A.* indicates *Psychological Abstracts).* Abbreviations for journals are those used in *A World List of Scientific Periodicals Published in the years 1900-1933,* 2nd Edition. For journals not listed, abbreviations were devised according to the general rules used in the above source. It is impossible to cover all journals and list all papers concerned with aging and the aged. Authors and publishers are requested to call attention to publications or to send reprints to the Gerontology Section, Baltimore City Hospitals, Baltimore, Md.

GERONTOLOGY

2178. Brull, L.: Première conférence internationale de gérontologie. *Rev. méd. Liège, 5:* 593-613, 1950.

2179. Derber, M. (Editor): *The aged and society.* Industr. Rel. Res. Ass., Champaign, Ill., 1950, vii, 237 pp.

2180. Dudley, S. F.: Gerontology or the problems of old age. *J. roy. nav. med. Serv., 36:* 111-124, 1950.

2181. Eckerström, S.: (Physiology of old age.) *Nord. Med., Stockholm, 9:* 1591-1595, 1948.

2182. Fromme, A.: Gedanken über Leben, Altern, Krankheit und Tod unter Zugrundelegung der Entwicklungsgeschichte. *Z. ges. innere Med., 5:* 321-330, 1950.

2183. Jalavisto, E.: *(Gerontology and geriatrics.) Suomen Lääkärilehti,* Helsinki, 1948, pp. 1-13.

2184. Jones, H. E. (Chairman): *Research on aging. Proceedings of a conference held on August 7-10, 1950, at the University of California, Berkeley.* Pacific Coast Comm. on Old Age Res., Soc. Sci. Res. Counc., N. Y., 1950, 128 pp.

2185. Kotsovsky, D.: Apologie des Alters. *Scientia, Milano, 42:* 133-144, 1948.

2186. Minkowski, E.: Problèmes d'adaptation au cours de la vieillesse. *Sem. Hôp. Paris, 26:* 2294-2295, 1950.

2187. Rabino, A.: Gerontologia e gerontoiatria. *Minerva med., Torino, 41:* 528-534, 1950.

2188. Southworth, W. H.: *Problems of an aging population in Wisconsin; a discussion guide for clubs, groups, and individuals.* Univ. Wisc., Univ. Ext. Div., Bur. Infor. & Prog. Serv., Madison, 1950, 16 pp.

2189. U. S. Federal Security Agency: *Some facts about our aging population.* Nat. Conf. on Aging, Wash., Aug. 1950, 15 pp.

2190. Zironi, A.: Nouvelle hypothese sur la physiogénie de la vieillesse. *Rev. méd. Liège, 5:* 683-686, 1950.

2191. Anonymous: Problems of old age. (Abstract of Symposium). *Nature, Lond., 163:* 221-223, 1949.

BIOLOGY OF AGING

I. CELLULAR BIOLOGY AND PHYSIOLOGY

2192. Berger, E. Y., M. F. Dunning, J. M. Steele, R. Jackenthal, and B. B. Brodie: Estimation of intracellular water in man. *Amer. J. Physiol., 162:* 318-325, 1950.

2193. Bourlière, F.: Sénescence et vitesse de cicatrisation chez le rat. *Rev. méd. Liège, 5:* 669-671, 1950.

2194. Bourlière, F., and M. Gourévitch: Âge et vitesse de réparation des plaies expérimentales chez le rat. *Arch. Biochem., 17:* 269, 1948.

2195. Bunting, H.: Interstitial desoxyribonucleic acid following cell death. *Yale J. Biol. Med., 22:* 521-525, 1950.

2196. Cole, J. W., D. T. Shaw, and P. Fraser: Wound healing; cutaneous and serum inhibition of hyaluronidase; an experimental study. *Surg., Gynec. Obstet., 90:* 269-274, 1950.

2197. Li, M. H., and W. U. Gardner: Influence of age of host and ovaries on tumorigenesis in intrasplenic and intrapancreatic ovarian grafts. *Cancer Res., 10:* 162-165, 1950.

2198. Rockstein, M.: The relation of cholinesterase activity to change in cell number with age in the brain of the adult worker honeybee. *J. cell. comp. Physiol., 35:* 11-23, 1950. Abstr: *B. A., 24:* No. 29194, 1950.

2199. Steele, J. M., E. Y. Berger, M. F. Dunning, and B. B. Brodie: Total body water in man. *Amer. J. Physiol., 162:* 313-317, 1950.

IV. Longevity

(heredity, diet, occupation, and sex differences)

2200. Aysoy, A.: Étude statistique de la mortalité à Ankara et à Istanbul durant les années allant de 1940 à 1944. *Rev. Path. comp., 50:* 427-434, 1950.

2201. Dickinson, F. G.: Preventable deaths. *Today's Hlth., 28:* 13, June 1950.

2202. Gerard, R. W.: Life that doesn't run down. *Sci. Digest, 26:* 57-59, Nov. 1949.

2203. Harris, H., and C. A. B. Smith: The sib-sib age of onset correlation among individuals suffering from a hereditary syndrome produced by more than one gene. *Ann. Eugen., Camb., 14:* 309-318, 1949.

2204. Jalavisto, E.: The influence of parental age on the expectation of life. *Rev. méd. Liège, 5:* 719-722, 1950.

2205. Kallmann, F. J.: Medical genetics and eugenics in relation to mental health problems and senescence. (Abstract). *Eugen. News, 33:* 15-17, 1948. Abstr: *P. A., 24:* No. 5925, 1950.

2206. Kallmann, F. J., and L. Feingold: Principles of human genetics in relation to insurance medicine and public health. *J. insur. Med., 4:* 1-8, 1949.

2207. Metrop. Life Insur. Co.: Longevity of industrial workers. *Statist. Bull. Metrop. Life Insur. Co., 31:* 4-7, Nov. 1950.

2208. Moine, M.: Morbidité et mortalité en fonction de l'activité professionnelle. *Médecin fr., 10:* 171-174, 1950.

2209. Rössle, R.: Warum sterben so wenig Menschen eines natürlichen Todes? *Experimentia, 4:* 295-303, 1948.

2210. Shellard, G. D.: Probability of death; reply. *Sci. Amer., 182:* 2, June 1950.

2212. Spiegelman, M.: *Health progress in the United States; a survey of recent trends in longevity.* Amer. Enterprise Ass., Inc., N. Y., 1950, 28 pp.

2213. Thomas, A.: Longévité et facteur travail. *Rev. méd. Liège, 5:* 729-730, 1950.

2214. Anonymous: Continued rise in longevity of industrial population. *Statist. Bull. Metrop. Life Insur. Co., 31:* 3-4, Aug. 1950.

2215. Anonymous: Lifespan may double in next ten years. *Sci. News Lett., Wash., 57:* 328, May 27, 1950.

2216. Anonymous: Married population at record high. *Statist. Bull. Metrop. Life Insur. Co., 31:* 3-5, July 1950.

2217. Anonymous: You inherit old age, twin study reveals. *Sci. News Lett., Wash., 54:* 182, Sept. 18, 1948.

See also No. 2465.

IV-C. Longevity: *Comparative Physiology*

2218. Blair, W. F.: Population density, life span, and mortality rates of small mammals in the blue-grass meadow and blue-grass field associations of southern Michigan. *Amer. Midl. Nat., 40:* 395-419, 1948.

2219. Coutelin, F., G. Biguet, and G. Cochet: La culture de *Trichomonas natricis.* Développement et longévité des colonies en fonction de la composition des milieux. *Bull. Soc. pathol. exot., 41:* 536-538, 1948.

2220. Deevey, E. S., Jr.: Probability of death; varies with age and species. *Sci. Amer., 182:* 58-60, Apr. 1950.

2221. Matheson, C.: Longevity in the grey seal. *Nature, Lond., 166:* 73-74, 1950.

2222. Stott, K.: Notes on the longevity of captive birds. *Auk, 65:* 402-405, 1948.

IV-H. Longevity: *Mortality Rates*

2223. Aiello, G.: Augmentation de la mortalité parmi les individus de plus de 65 ans (1936-1948) avec considérations particulières sur certaines maladies caractéristiques. *Rev. méd. Liège, 5:* 715-716, 1950.

2224. Löwe, H.: Der Sterblichkeitsrückgang und seine Folgen für die Ärzteschaft. *Dtsch. med. Wschr., 75:* 1230-1231, 1950.

2225. Tallybrass, C. O.: Evolution of disease; with particular reference to variations in age-incidence and mortality. *Mon. Bull. Min. Hlth. Lab. Serv., Lond., 7:* 120-127, June 1948.

2226. U. S. Federal Security Agency. Public Health Service. Office of Vital Statistics: Estimated numbers of deaths and death rates for specified causes; United States, 1949. *Current Mortality Analysis, 7:* (13), 3-18, 1950.

2227. U. S. Federal Security Agency. Public Health Service. Office of Vital Statistics: Deaths and death rates for selected causes by age, race, and sex; United States, 1948. *Vit. Statist., Spec. Rep., National Summaries, 35:* (18), 315-345, 1950.

2228. Anonymous: Cancer, Tuberculose et Longevité. *Progr. méd., Paris, 76:* 453, 1948.

See also No. 2513.

V. Metabolism

2229. Albright, F., and E. C. Reifenstein, Jr.: *Parathyroid glands and metabolic bone diseases; selected studies.* Williams & Wilkins Co., Baltimore, 1948, 393 pp.

2230. Axelsson, J., and S. Eriksson: Factors influencing the calcium and phosphorous metabolism of adult sheep. *Kungl. Lantbrukshögskolans Ann., 16:* 711-722, 1949. Abstr: *B. A., 24:* No. 22813, 1950.

2231. Goldman, J. M. D.: Effect of cholesterol feeding in hamsters. *Arch. Path., Chicago, 49:* 169-172, 1950. Abstr: *B. A., 24:* No. 22869, 1950.

2232. Hellman, L. M., B. A. Harris, Jr., and M. C. Andrews: Studies of the metabolism of the human placenta; oxygen consumption and anaerobic glyolysis in relation to aging and severe toxemia *Johns Hopk. Hosp. Bull., 87:* 203-214, 1950.

2233. Lee, D. H. R. L.: *Physiology of tissues and organs.* C. C. Thomas Publ. Co., Springfield, 1950, 159 pp.

2234. Millen, R. S., and J. Hindman: Daily variations in basal metabolic recordings throughout the entire menstrual cycle determined at home under ideal circumstances. *Med. Times, N. Y., 78:* 350-352, 1950.

2235. Moreton, J. R.: Chylomicronemia, fat tolerance, and atherosclerosis. *J. Lab. clin. Med., 35:* 373-384, 1950. Abstr: *B. A., 24:* No. 26176, 1950.

2236. Osserman, E. F., G. C. Pitts, W. C. Welham, and A. R. Behnke: In vivo measurement of body fat and body water in a group of normal men. *J. appl. Physiol., 2:* 633-639, 1950.

2237. Schilling, A., and D. Laszlo: The effect of diethylstilbestrol on the calcium, phosphorus and nitrogen metabolism of prostatic carcinoma. *J. clin. Invest., 29:* 918-924, 1950.

2238. Schloerb, P. R., B. J. Friis-Hansen, I. S. Edelman, A. K. Solomon, and F. D. Moore: The measurement of total body water in the human subject by deuterium oxide dilution; with a consideration of the dynamics of deuterium distribution. *J. clin. Invest., 29:* 1296-1310, 1950.

2239. Soskin, S.: Role of the endocrines in the regulation of blood sugar. *J. clin. Endocrinol., 4:* 75-88, 1944.

2240. Tunbridge, R. E., and E. C. Allibone: The intravenous dextrose tolerance test. *Quart. J. Med., 9:* 11-35, 1940.

2241. Woods, R.: Cholesterol. *Borden's Rev. nutrit. Res., 11:* 79-90, Oct. 1950.

2242. Anonymous: (Conference on modification of metabolism and reactivity of the organism with age.) *Arkh. Pat., Moskva, 12:* (5), 95-96, 1950.

See also Nos. 2199, 2237, 2248, 2271, 2272, 2283, 2352, 2476, 2662.

VI. Nutrition

2243. Barnes, B. C., E. E. Wollaeger, and H. L. Mason: The comparative absorption of vitamin A from a water-miscible and an oily preparation by normal human adults and patients with steatorrhea. *J. clin. Invest., 29:* 982-987, 1950.

2244. Chieffi, M., and J. E. Kirk: Vitamin studies in middle-aged and old individuals. V. Hypovitaminemia B_1. Effect of thiamine administration on blood thiamine concentration and clinical signs and symptoms. *J. Geront., 5:* 326-330, 1950.

2245. DeCourcy, J. L.: Practical nutrition of the geriatric patient. *Geriatrics, 3:* 353-360, 1948.

2246. Fearon, W. R.: Nutritional errors in old age. *J. med. Ass. Eire, 27:* 41-42, Sept. 1950.

2247. Irving, J. T.: The dietary calcium requirements of man. *S. Afr. med. J., 24:* 601-606, 1950.

2248. Jansen, B. C. B.: Voeding, stofwisseling en ouderdom. *Ned. Tijdschr. Geneesk., 94:* 2045-2046, 1950.

2249. Jansen, B. C. B.: The necessity of vitamin D in old age. *Rev. méd. Liège, 5:* 667-669, 1950.

2250. Langley, G. J.: Diet in old age. *Practitioner, 165:* 148-155, 1950.

2251. Ohlson, M. A., L. Jackson, J. Boek, D. C. Cederquist, W. D. Brewer, E. G. Brown, J. Traver, M. M. Lott, M. Mayhew, D. Dunsing, and H. Tobey: Nutrition and dietary habits of aging women. *Amer. J. publ. Hlth., 40:* 1101-1108, 1950.

2252. Oldham, H.: Dietary needs of special age groups. *Milk Dealer, 38:* (5), 45-46; 118-122, 1949. Abstr: *B. A., 24:* No. 17766, 1950.

2253. Solá, O. H., and N. Serantes: Carencias habituales en las gravidas, en la madre lactante y en la senectud. *Rev. Asoc. méd. Argent., 63:* 23-38, 1949.

2254. Stambovsky, L.: Nutrition and geriatrics. *Drug & Cosmetic Ind., 56:* 6, June 1945.

2255. Trulson, M., J. Ogle, and F. J. Stare: New York State nutrition survey. III. A study of one week's food purchases of 135 families. *J. Amer. diet. Ass., 25:* 764-769, 1949. Abstr: *B. A., 24:* No. 22883, 1950.

2256. Vinther-Paulsen, N.: Investigations of the actual food intake of elderly chronically hos-

pitalized patients. *J. Geront., 5:* 331-338, 1950.

2257. Vinther-Paulsen, N.: Glossitis as indicator of nutritional deficiency in the aged. *Rev. méd. Liège, 5:* 652-654, 1950.

2258. Anonymous: Desirable fat levels in the diet. *Nutrit. Rev., 8:* 232-233, 1950.

2259. Anonymous: Diet and arteriosclerosis. *Nutrit. Rev., 6:* 99-101, 1948.

2260. Anonymous: Old people in homes may not get vitamins. *Sci. News Lett., Wash., 58:* 281, Oct. 28, 1950.

See also Nos. 2284, 2339, 2433, 2673.

VII. Parental Age

2261. Lowe, C. R., and T. McKeown: The sex ratio of human births related to maternal age. *Brit. J. soc. Med., 4:* 75-85, 1950.

See also No. 2204.

X. Theories

2262. Abderhalden, E.: Wandlungen in der Auffassung des Wesens der Alternsvorgänge. *Bull. schweiz. Acad. med. Wiss., 6:* 102-114, 1950.

2263. Bellman, R., and T. Harris: On the theory of age-dependent stochastic branching processes. *Proc. nat. Acad. Sci., Wash., 34:* 601-604, 1948.

See also No. 2190.

ORGAN SYSTEMS

I. Blood

2264. Antognetti, L.: L'activité de l'institut au sujet de la gérontologie et de la gériatrie. *Rev. méd. Liège, 5:* 732, 1950.

2265. Holmes, E. G., F. L. Gee, S. B. Asea, S. Bhima, W. K. Chagula, T. R. Evelia, J. W. S. Kasirye, G. H. Kiboneka, M. Y. Lugazia, M. Majale, M. S. Mughairy, E. C. Ochieng, J. I. H. Gesa, and J. C. Magambo: Red blood count of East African students. *East Afr. med. J., 27:* 196-206, 1950.

2266. Nizet, A.: Nutrition et longévité des hématies *Rev. méd. Liège, 5:* 679-683, 1950.

I-A. Blood: *Chemistry*

2267. Boselli, A., G. Mars, and M. Morpurgo: Les altérations protéinémiques dans la vieillesse. Recherches par les méthodes des (constellations) de réactions et de l'électrophorèse. *Rev. méd. Liège, 5:* 655-659, 1950.

2268. Dahl, S.: Serum magnesium in normal men and women. *Acta haemat., 4:* 65-72, 1950.

2269. Ferreira, F. A. G., and J. P. Ribeiro: Valores normais de sodio e potassio no soro sanguineo. *Amatus Lusitanus, 7:* 415-421, 1950.

2270. Gertler, M. M., S. M. Garn, and E. F. Bland: Age, serum, cholesterol and coronary artery disease. *Circulation, 2:* 517-522, 1950.

2271. Gertler, M. M., S. M. Garn, and J. Lerman: The interrelationships of serum cholesterol, cholesterol esters and phospholipids in health and in coronary artery disease. *Circulation, 2:* 205-214, 1950.

2272. Gertler, M. M., S. M. Garn, and H. B. Sprague: Cholesterol, cholesterol esters and phospholipids in health and in coronary artery disease; morphology and serum lipids in man. *Circulation, 2:* 380-391, 1950.

2273. Gofman, J. W., H. B. Jones, F. T. Lindgren, T. P. Lyon, H. A. Elliott, and B. Strisower: Blood lipids and human atherosclerosis. *Circulation, 2:* 161-178, 1950.

2274. Gokhale, S. H., and R. J. Lokre: Some constituents in normal blood in central India; serum proteins, serum albumin, serum globulin and serum non-protein nitrogen. *Indian med. Gaz., 85:* 94-96, 1950.

2275. Hofstatter, L., P. G. Ackermann, and W. B. Kountz: The plasma levels of nine free amino acids in old men and women. *J. Lab. clin. Med., 36:* 259-265, 1950.

2276. Keys, A., O. Michelsen, E. v. O. Miller, E. R. Hayes, and R. L. Todd: The concentration of cholesterol in the blood serum of normal man and its relation to age. *J. clin. Invest., 29:* 1347-1353, 1950.

2277. Lawrence, W. J.: The carbonic anhydrase content of the blood of one hundred normal Australian subjects. *Med. J. Aust., 34:* 587-589, 1947. Abstr: *B. A., 24:* No. 17626, 1950.

2278. LoBo-Parga, G., M. Madrid, and L. Gostin: Estudio electroforetico de las proteinas del suero y plasma de individuos normales. *Rev. méd. Chile, 77:* 686-689, 1949. Abstr: *B. A., 24:* No. 17628, 1950.

2279. McCance, R. A., A. O. Hutchinson, R. F. A. Dean, and P. E. H. Jones: The cholinesterase activity of the serum of newborn animals, and colostrum. *Biochem. J., 45:* 493-496, 1949. Abstr: *B. A., 24:* No. 17488, 1950.

2280. Morse, M., D. E. Cassels, M. Holder, E. O'Connell, and A. Swanson: The position of the oxygen dissociation curve of the blood in normal children and adults. *J. clin. Invest., 29:* 1091-1097, 1950.

2281. Olbrich, O.: Blood changes in the aged. *Indian med. Gaz., 84:* 121, 1949. Also *in: Edinb. med. J., 55:* 100, 1948.

2282. Quinn, R. W.: The antihyaluronidase content

of blood serum; a study of sera from patients with rheumatic fever, streptococcal infection, miscellaneous non-streptococcal diseases, and from normal individuals of different ages. *Ann. N. Y. Acad. Sci., 52:* 1118-1124, 1950.

2283. Reimer, A., E. Blecha, and C. F. Wilkinson, Jr.: Study of essential familial hypocholesterolemia; relationship of diet and blood cholesterol level. *J. Amer. diet. Ass., 25:* 842-844, 1949. Abstr: *B. A., 24:* No. 26228, 1950.

2284. Schettler, G.: Zum Einfluss der Ernährung auf den Cholesteringehalt des Blutes. *Klin. Wschr., 28:* 565-566, 1950.

2285. Sols, A.: Valoración de las proteínas del suero por referencia a la media normal. *Laboratorio, 9:* (54), 509-520, 1950.

2286. Wilkinson, C. F., Jr.: Essential familial hypercholesterolemia; cutaneous, metabolic and hereditary aspects. *Bull. N. Y. Acad. Med., 26:* 670-685, 1950.

2287. Wolff, H.: Der normale Zinkgehalt in Blut, Serum und Eythrocyten. *Dtsch. Arch. klin. Med., 197:* 263-267, 1950.

See also Nos. 2327, 2328, 2579.

I-B. Blood: *Coagulation*

2288. Baumüller, E.: Über die Prophylaxe der Thromboembolien. *Med. Klinik, 45:* 929-931, 1950.

2289. Blecha, C. V.: Behandlung von Thrombosen und Embolien mit Ultraschallwellen. *Wien. klin. Wschr., 62:* 480-481, 1950.

2290. Davis, P. B.: Thrombosis of the internal cerebral veins of Galen; report of two cases involving adults. *J. Amer. osteop. Ass., 50:* 21-22, 1950.

2291. Fryd, C. H., A. De Vries, E. Gitelson, K. Galewski, and E. Heiman-Hollaender: Prophylaxis and therapy of thrombo-embolism with anticoagulants. *Acta. med. orient., 9:* 105-122, 1950.

2292. Jürgens, J.: Erfahrungen mit Dicumarol in der inneren Medizin. *Ärztl. Wschr., 5:* 405-411, 1950.

2293. Kay, J. H., G. Balla, S. B. Hutton, and A. Ochsner: The prophylaxis of intravascular clotting by the use of alpha tocopherol and calcium. *N. Orleans med. surg. J., 103:* 116-120, 1950.

2294. Koller, F.: Die Prophylaxe und Therapie der Thrombose mit Antikoagulantien. *Helv. med. acta, 16:* 220-239, 1949. Abstr: *B. A., 24:* No. 17624, 1950.

2295. Leonhartsberger, F., and J. Schmid: Zur intravenösen Thrombokinasetherapie. *Wien. klin. Wschr., 62:* 437-443, 1950.

2296. Libánský, J., B. Polák, and Z. Dienstbier: (Clinical experiences with dicumarol therapy of coronary thrombosis.) *Čas. Lék. čes., 89:* 905-912, 1950.

2297. Ochsner, A., M. E. DeBakey, and P. T. DeCamp: Venous thrombosis. *J. Amer. med. Ass., 144:* 831-834, 1950. Also *in: J. Fla. med. Ass., 37:* 79-82, 1950.

2298. Overman, R. S., A. A. Newman, and I. S. Wright: Plasma prothrombin times in normal human subjects. The effect of certain factors on the prothrombin time. *Amer. Heart J., 39:* 56-64, 1950. Abstr: *B. A., 24:* No. 26909, 1950.

2299. Raevskaia, G. V.: (Thrombosis and embolism of peripheral arteries in myocardiac infarct.) *Sovetsk. Med.,* (9), 9-11, Sept. 1950.

2300. Tareev, E. M.: (Pathogenesis and treatment of thromboembolic diseases.) *Sovetsk. Med.,* (9), 6-9, Sept. 1950.

2301. Zannini, G.: Sulle trombosi venose e sul loro trattamento con anticoagulanti. *Policlinico. (Sez. prat.), 57:* 997-1005, 1950.

2302. Zuckermann, R., A. Bisteni, J. Ortiz, and D. Sodi Pallares: Flebotrombosis y tromboflebitis coronarias. *Arch. Inst. Cardiol. México, 20:* 286-296, 1950.

2303. Anonymous: Tratamiento de la trombosis venosa. *Día méd., 22:* 1870-1872, 1950.

See also Nos. 2317, 2331, 2342, 2344.

II. Blood Forming and Destroying Organs

2304. Ferrand, B.: L'hématopoièse chez l'adulte; aspects cytologiques, biochimiques et physiologiques. *Cah. méd., Alger, 5:* 531-555, 1950.

2305. Giordano, A., and V. Cheli: La moelle osseuse et le sang périphérique dans la sénilité. *Rev. méd. Liège, 5:* 683, 1950.

III. Cardiovascular System

(blood vessels, blood pressure, hypertension, blood volume, veins, and arteriosclerosis)

2306. Alexander, H. A.: Fundamental principles in the treatment of varicose veins. *Minn. Med., 33:* 626-628, 1950.

2307. Baldwin, D., C. B. Taylor, and G. M. Hass: A comparison of arteriosclerotic lesions produced in young and in old rabbits by freezing the aorta. *Arch. Path., Chicago, 50:* 122-131, 1950.

2308. Barker, N. W.: The diagnosis and treatment of chronic occlusive disease of the peripheral arteries. *Wis. med. J., 49:* 470-474, 1950.

2309. Boyd, A. M.: The diagnosis and pathogenesis of obliterative vascular disease of the lower extremities. *Angiology, 1:* 373-390, 1950.

2310. Bradfield, J. Y., and M. R. Hejtmancik: Cardiac disease and rheumatoid arthritis. *Arch. intern. Med., 86:* 1-9, 1950.

2311. Calhoun, C. W., and J. R. Broun: The problem of varicose veins. *Northw. Med., Seattle, 49:* 467-469, 1950.

2312. Cambra Mercader, R., and J. Cuxart Bartoli: Interés del estudio de la velocidad de circulación en el viejo. *Acta méd. hisp., 8:* (61-62), 46-49, 1950.

2313. Cassel, M. A.: Treatment of post-thrombotic syndrome by interruption of superficial femoral vein. *Arch. Surg., Chicago, 61:* 540-553, 1950.

2314. Coppo, M.: Pathogénie de l'athérosclérose. *Rev. méd. Liège, 5:* 628-631, 1950.

2315. Dotter, C. T., D. J. Roberts, Jr., and I. Steinberg: Aortic length; angiocardiographic measurements. *Circulation, 2:* 915-920, 1950.

2316. Duguid, J. B.: Pathogeny of arteriosclerosis. *Rev. méd. Liège, 5:* 618-619, 1950.

2317. Eckl, E., and F. Leibetseder: Thrombophlebitis saltans und Phlebothrombose. *Wien. klin. Wschr., 62:* 420-422, 1950.

2318. Edwards, E. A.: Thromboangiitis obliterans in women; possible relation to rheumatic disease. *New Engl. J. Med., 243:* 290-294, 1950.

2319. Faust, F. B.: The no man's range of normal blood pressure; based on biometric charts of 6,500 readings over 20 years (1928-1948). *Miss. Valley med. J., 72:* 130-133, 1950.

2320. Fiehrer, A.: Conduite à tenir enprésence d'une phlébite. *Clinique, Paris, 45:* 15-22, 1950.

2321. Field, A.: Varicose veins; early studies and treatments. *Ann. west. Med. Surg., 4:* 403-406, 1950.

2322. Formijne, P.: Ouderdom en bloedvaten. *Ned. Tijdschr. Geneesk., 94:* 2046-2052, 1950.

2323. Froehlich, F., and M. Conrath: Indications des ligatures veineuses dans le traitement des troubles artériels periphériques. *Lyon chir., 45:* 614-618, 1950.

2324. Fulton, J. S., and B. A. McSwiney: The pulse wave velocity and extensibility of the brachial and radial artery in man. *J. Physiol., 69:* 386-392, 1930.

2325. Geiringer, E.: The gerontological aspects of atheroma. An approach to a pathology of senescence. *Brit. J. soc. Med., 2:* 132-138, 1948.

2326. Geiringer, E.: L'artériosclérose en tant que phénomène propre au vieillissement. *Rev. méd. Liège, 5:* 614-618, 1950.

2327. Gregersen, M. I.: Physiological characteristics of the Chinese. I. Plasma volume, blood volume, available fluid (NaSCN), hematocrit value, plasma protein level and oxygen capacity and carbon monoxide content of the blood in normal Chinese males. *Chin. J. Physiol., 17:* 35, 1949. Abstr: *B. A., 24:* No. 17618, 1950.

2328. Gregersen, M. I.: Physiological characteristics of Chinese. II. Plasma volume, blood volume, available fluid (NaSCN), hematocrit value, plasma protein level and oxygen capacity and carbon monoxide content of the blood in Chinese normal females. *Chin. J. Physiol., 17:* 73, 1949. Abstr: *B. A., 24:* No. 17619, 1950.

2329. Hirsch, S.: L'artériosclérose dans le cadre de la gérontologie moderne. *Rev. méd. Liège, 5:* 633-636, 1950.

2330. Hueper, W. C.: Prevention and treatment of atherosclerosis. *Med. Clin. N. Amer., N. Y* pp., 773-781, May 1949.

2331. Kinmonth, J. B.: Arteriosclerosis; thrombosis of iliac arteries. *Proc. roy. Soc. Med., 43:* 480-481, 1950.

2332. Kotsovsky, D.: Abriss der Therapie des Zirkulationssystems im Alter. *Med. Mschr., 4:* 401-405, 1950.

2333. Lamming, R. L.: The modern treatment of varicose veins. *Med. Pr., 224:* 243-247, 1950.

2334. Lansing, A. I., M. Alex, and T. B. Rosenthal: Atheromatosis as a sequel to senescent changes in the arterial wall. *J. Geront., 5:* 314-318, 1950.

2335. McPheeters, H. O.: Resume of present-day care and treatment of varicose veins and their complications. *Minn. Med., 33:* 628-629, 1950.

2336. Master, A. M., L. I. Dublin, and H. H. Marks: The normal blood pressure range and its clinical implications. *J. Amer. med. Ass., 143:* 1464-1470, 1950.

2337. Mininni, G., and G. Scardigli: Aspects métaboliques de la diathèse thrombophilique. *Rev. méd. Liège, 5:* 659-660, 1950.

2338. Morrison, L. M., and K. D. Johnson: Cholesterol content of the coronary arteries and blood in acute coronary artery thrombosis. *Amer. Heart J., 39:* 31-34, 1950. Abstr: *B. A., 24:* No. 26904, 1950.

2339. Moses, C., and G. M. Longabaugh: Evaluation of choline in the prevention of experimental atherosclerosis; importance of changes in body weight. *Arch. Path., Chicago, 50:* 179-182, 1950.

2340. Moses, C., and G. M. Longabaugh: Effect of potassium iodide on aortic atherosclerosis in rabbits. *Geriatrics, 5:* 310-313, 1950.

2341. Nieuwmeijer, A. H., and K. Brandsma: Blood pressure levels in the Netherlands during the war. *Arch. intern. Med., 83:* 429-451, 1949.

2342. Olivier, C.: Pour le traitement anticoagulant des phlébites récentes du membre inférieur. *Pr. méd., 58:* 793-794, 1950.

2343. Pollak, O. J.: Plasmatic dyscolloidity as cause of atherosclerosis. *Rev. méd. Liège, 5:* 619-628, 1950.

2344. Prat, D., and A. Garcia Guelfi: Flebitis y trombosis venosas. *An. Fac. Med. Montevideo, 35:* 219-246, 1950.

2345. Rabboni, F.: Sul trattamento della tromboangioite obliterante. *Sicilia San., 7:* 209-216, 1950.

2346. Ruggiero, A.: La terapia della sindrome postflebitica dell'arto inferiore. *G. ital. Chir., 6:* 507-511, 1950.

2347. Scardigli, G., G. Mininni, and P. Capelli: Traitement associé: Propionate de testostérone-Vitamine E, et athérosclérose provoquée chez le lapin. *Rev. méd. Liège, 5:* 631-633, 1950.

2348. Servelle, M.: Étude de 420 cas de séquelles de phlébites. *Sem. Hôp. Paris, 26:* 2483-2487, 1950.

2349. Sinapius, D.: Zur Genese atherosklerotischer Frühveränderungen der Aorta. *Virchows Arch., 318:* 316-351, 1950.

2350. Smith, C., and L. A. Loewenthal: A study of elastic arteries in irradiated mice of different ages. *Proc. Soc. exp. Biol., N. Y., 75:* 859-861, 1950.

2351. Stürup, H., and I. C. Højensgard: Venous pressure in varicose veins in patients with incompetent communicating veins; a study of the statics and dynamics of the venous system of the lower extremity under pathological conditions. *Acta chir. scand., 99:* 518-536, 1950.

2352. Thannhauser, S. J.: Is there a relationship in pathogenesis between arteriosclerosis and familial hypercholesteremia? *Bull. N. Eng. med. Center, 12:* 129-133, 1950.

2353. Wellman, W. E., and J. E. Edwards: Thickness of the media of the thoracic aorta in relation to age. *Arch. Path., Chicago, 50:* 183-188, 1950.

2354. White, P. D., E. G. Dimond, and A. Williams: Follow-up study of one hundred private hypertensive patients with cardiovascular complications. *J. Amer. med. Ass., 143:* 1311-1317, 1950.

2355. Anonymous: Atherosclerosis and serum cholesterol fractions. *Nutrit. Rev., 8:* 176-178, 1950.

See also Nos. 2235, 2271, 2273, 2301, 2303, 2470.

III-G. Cardiovascular System: *Heart*

(heart, anatomy and physiology; heart disease, coronary artery disease, and myocardial disease)

2356. Adlersberg, D., A. D. Parets, and E. P. Boas: Studies of families with xanthoma and unselected patients with coronary artery disease under the age of fifty years. *J. Amer. med. Ass., 141:* 246-254, 1949. Abstr: *B. A., 24:* No. 12494, 1950.

2357. Ambrust, C. A., Jr., and S. A. Levine: The treatment of angina pectoris with a preparation of khellin *(amni visnaga). Amer. J. med. Sci., 220:* 127-132, 1950.

2358. Askey, J. M., and J. E. Kahler: Longevity in extensive organic heart lesions; a case of Lutembacher's syndrome in a man aged 72. *Ann. intern. Med., 33:* 1031-1036, 1950.

2359. Calandre Díaz, L.: El dolor de la angina de pecho e infarto del miocardio. *Medicamenta, Madrid, 8:* 247-249, 1950.

2360. Cloyd, A. D.: Cardiac problems of geriatrics. *Neb. St. med. J., 35:* 256-258, 1950.

2361. Crain, R. B., M. E. Missal, and K. W. Wilson: The industrial employee with myocardial infarction; his ability to return to work. *Arch. industr. Hyg. & occup. Med., 1:* 525-538, 1950.

2362. Currens, J. H.: Common cardiac conditions in the young male adult. *J. Aviat. Med., 21:* 259-264, 1950.

2363. Defilippo, R.: Ateroesclerosis de las arterias coronarias cardiacas. *Arch. Soc. argent. Anat. norm. patol., 9:* 287-296, 1947. Abstr: *B. A., 24:* No. 26854, 1950.

2364. Ellis, F. R., M. Greaves, and H. H. Hecht: Congenital heart disease in old age; interauricular septal defect with mitral and tricuspid valvulitis. *Amer. Heart J., 40:* 154-161, 1950.

2365. France, R.: The use of quinidine in the treatment of cardiac arrhythmias. *Amer. Practit., 1:* 790-791, 1950.

2366. Freeman, Z.: The electrocardiogram in old age. *Med. J. Aust., 1:* (15), 499-503, 1950.

2367. Geill, T.: Calcification of the left annulus fibrosus (230 cases). *Rev. méd. Liège, 5:* 639-642, 1950.

2368. Gibson, P. C.: The ageing heart. *Practitioner, 165:* 115-123, 1950.

2369. Irvin, C. W., Jr., and A. M. Burgess, Jr.: The abuse of bed rest in the treatment of myocardial infarction. *New Engl. J. Med., 243:* 486-489, 1950.

2370. Jayne, E. P.: Cytochemical studies of age pigments in the human heart. *J. Geront., 5:* 319-325, 1950.

2371. Luciani, A., and F. Ferri: La dinamica del cuore nel soggetto normale; (studio grafico-cronometrico dei tempi della sistole). *Rass. Fisiopat. clin. terap., 22:* 75-101, 1950.

2372. Maresh, M. M.: Growth of the heart related to bodily growth during childhood and adolescence. *Pediatrics, 2:* 382-404, 1948. Abstr: *B. A., 24:* No. 18035, 1950.

2373. Martinez Gonzales, M.: Tratamiento de la angina de pecho. *Día méd., 22:* 2626-2631, 1950.

2374. Oliver, B. B., S. Eisenberg, T. Lombardo, and W. Viar: Alterations in sodium excretion, glomerular filtration and cardiac output in normal subjects. *J. clin. Invest., 29:* 837, 1950.

2375. Schierge, M.: Herzmuskelerkrankungen und Arbeitsfähigkeit. *Deut. Gesundhwes., 5:* 984-988, 1950.

2376. Smith, K. S.: The failing heart. *Brit. med. J., 2:* 340-342, 1950.

2377. Stubbs, J. B., and R. D. Woolsey: Angina pectoris; treatment by injection of stellate ganglia with ammonium sulfate. *Sth. med. J., Birmingham, 43:* 675-677, 1950.

2378. Switzer, J. L.: The differentiation of angina pectoris, chronic coronary insufficiency, and myocardial infarction. *Amer. Practit., 1:* 828-839, 1950.

2379. Tizzano, A.: La mortalité par maladies de l'appareil circulatoire. *Rev. med. Liège, 5:* 642-644, 1950.

2380. von Albertini, A.: Relations entre les sténoses valvulaires calcifées et les endocardites. *Rev. méd. Liège, 5:* 637-639, 1950.

2381. White, P. D., J. W. Hurst, and R. H. Fennell: Survival to the age of seventy-five years with congenital pulmonary stenosis and patent foramen ovale. *Circulation, 2:* 558-564, 1950.

2382. Wroblewski, F., and W. J. Messinger: Active rheumatic carditis in patients over 40 years of age. *Amer. Heart J., 40:* 345-353, 1950.

See also Nos. *2270, 2272, 2296, 2302.*

IV. Connective Tissue and Cartilage

2383. Castiglioni, G., and P. Peregalli: Su alcune caratterististiche biologiche e strutturali della cartilagine articolare umana. *Arch. Ortop., 63:* 36-58, 1950.

2384. Feitelberg, S., and P. E. Kaunitz: X-ray diffraction studies of human *chordae tendineae. Biochim. biophys. Acta, 3:* 155-160, 1949. Abstr: *B. A., 24:* No. 9660, 1950.

2385. Gross, J.: Connective tissue fine structure and some methods for its analysis. *J. Geront., 5:* 343-360, 1950.

2386. Gross, J.: Aging changes in the collagenous connective tissue of rat skin. *J. nat. Cancer Inst., 10:* 1353, 1950.

2387. Hegemann, G., I. Nickell, and F. Tischler: Beobachtungen über den Wechsel in der Doppelbrechfähigkeit und der Trypsinresistenz kollagener Fasern beim Altern von Narbengewebe. *Klin. Wschr., 28:* 362-364, 1950.

2388. Pratt, A. W., and R. W. G. Wyckoff: The fine structure of connective tissue fibrils. *Biochim. et biophys. Acta, 5:* 166-174, 1950.

2389. Roncallo, P.: Researches on the ossification and conformation of the thyroid cartilage in man. *Acta oto-laryng., Stockh., 36:* 110-134, 1948. Abstr: *B. A., 24:* No. 6413, 1950.

2390. Wolpers, C.: Elektronenmikroskopische Untersuchungen zur Pathologie kollagener Fasern. *Frankfurt. Z. Path., 61:* 417-429, 1950.

V. Endocrine System

(includes sex glands and climacteric)

2391. Atria, A.: La menopausia precoz y su tratamiento hormonal. *Rev. méd. Chile, 78:* 373-377, 1950.

2392. Bourg, R., and P. Pundel: Étude des frottis vaginaux post-ménopausiques. *Rev. méd. Liège, 5:* 691-693, 1950.

2393. Cachera, R., M. Lamotte, and N. Masse: Syndrome basedowien post-ménopausique guéri par les oestrogènes; changements observés dans les liquides extra-cellulaires. *Paris méd., 40:* 347-351, 1950.

2394. Cervellati, L.: Epifisi e menopausa. *Ann. Ostet. Ginec., 72:* 239-251, 1950.

2395. Decourt, J., J. Gruner, and J. Lapresle: Les lésions cérébrales du myxoedème; à propos de deux observations de myxoedème tardif chez l'adulte. *Ann. Mèd., 51:* 352-378, 1950.

2396. Dublineau, J.: Problèmes d'adaptation à la ménopause. *Sem. Hôp. Paris, 26:* 2287-2290, 1950.

2397. Fontan Balestra, E.: Climaterio y alergia. *Sem. méd., B. Aires, 57:* 1149-1152, 1950.

2398. Gougerot, H., B. Duperrat, and L. Hartmann: Syndrome de Raynaud de la ménopause et concrétions calcaires. *Bull. Soc. méd. Hôp. Paris, 66:* 1125-1127, 1950.

2399. Greppi, E.: Au sujet de la ménopause comme point de départ de la pléthore vasculaire discrasique. *Rev. méd. Liège, 5:* 693-697, 1950.

2400. Gusso, A.: Le artropatie della menopausa e la loro cura. *Accad. Med., Torino, 65:* 57-74, 1950.

2401. Herschberg, A. D.: Le syndrome hyperhormonal de la préménopause. *Clinique, Paris, 45:* (428), 3-17, 1950.

2402. Jorda Serra, E. A.: Atropatías de la rodilla en el climaterio. *Medicamenta, Madrid, 8:* 258-259, 1950.

2403. Jost, A., and R. A. Colonge: Greffe de testicule foetal de rat sur l'adulte castré et hypophysectomisé. Remarques sur la physiologie du testicule foetal de rat. *C. R. Soc. Biol., Paris, 143:* 140-142, 1949. Abstr: *B. A., 24:* No. 23211, 1950.

2404. Jutoran, M.: Diabetes y vejez. *Prensa méd. argent., 37:* 1519-1522, 1950.

2405. Knierer, W.: Impetigo herpetiformis bei einer Frau jenseits des Klimakteriums. *Derm. Wschr., 122:* 652, 1950.

2406. Korenchevsky, V.: Rejuvenative, or eliminative and preventive treatment of senility, as suggest-

ed by experiments on rats. *Rev. méd. Liège, 5:* 687-691, 1950.

2407. Korenchevsky, V., and S. K. Paris: Co-operative effects of endocrinological factors and processes of ageing in producing adenoma-like structures in rats. *Cancer, 3:* 903-922, 1950.

2408. Kotek, A.: Die Röntgenkastration bei klimakterischen Blutungen. *Zbl. Gynäk., 72:* 732-737, 1950.

2409. Kountz, W. B., M. Chieffi, and J. E. Kirk: An evaluation of thyroid function in older individuals with various degrees of arteriosclerosis. *Amer. Heart J., 36:* 475, 1948.

2410. Kowalewski, K.: Les variations quotidiennes d'élimination de 17-cétostéroïdes urinaires neutres chez l'homme. *Ann. Endocrin., Paris, 11:* 82-87, 1950.

2411. Mandl, A. M., and S. Zuckerman: The numbers of normal and atretic ova in the mature rat. *J. Endocr., 6:* 426-435, 1950.

2412. Marks, J. H., and M. H. Wittenborg: Results of treatment of carcinoma of the ovary with data on the age incidence of this disease. *Surg., Gynec. Obstet., 87:* 541-545, 1948.

2413. Masters, W. H., and D. T. Magallon: Androgen administration in the postmenopausal woman. *J. clin. Endocrinol., 10:* 348-358, 1950. Abstr: *B. A., 24:* No. 26666, 1950.

2414. Nilsson, B.: The normal size of sella turcica. *Acta genet., Basel, 1:* 355-360, 1949-1950.

2415. Pan, S.-Y., H. Kaunitz, and C. A. Slanetz: Restoration of vaginal estrous by alphatocopheryl acetate in old rats. *Ann. N. Y. Acad. Sci., 52:* 80-82, 1949. Abstr: *B. A., 24:* No. 26308, 1950.

2416. Perloff, W. H.: The female climacteric. *J. insur. Med., 5:* (3), 32-35, 1950.

2417. Plate, W. P.: Functional uterine hemorrhage at the menopause caused by oestrogenic substances from the cortex of the adrenal gland. *Acta endocrinol., 4:* 363-373, 1950.

2418. Quimby, E. H., S. C. Werner, and C. Schmidt: Influence of age, sex, and season upon radioiodine uptake by the human thyroid. *Proc. Soc. exp. Biol., N. Y., 75:* 537-540, 1950.

2419. Sniffen, R. C.: The testis. I. The normal testis. *Arch. Path., Chicago, 50:* 259-284, 1950.

2420. Tarnopolsky, S., E. Montuori, and M. Schere: Eliminación de 17-cetosteroides en gota. *Prensa méd. argent., 37:* 1778-1779, 1950.

2421. Tausk, M.: Endocrinologie en ouderdom. *Ned. Tijdschr. Geneesk., 94:* 2042-2044, 1950.

2422. Van Meensel, F.: Que signifient les hémorragies du retour de couches au point de vue endocrinien? Étude des frottis vaginaux combinés aux biopsies endométriales. *Gynéc. et Obstét., 49:* 241-255, 1950.

2423. Vignes, H.: Métrorrhagies après la ménopause. *J. Prat., Paris, 64:* 355, 1950.

2424. Wagner, H.: Genitale Blutungen in der Menopause mit besonderer Berücksichtigung der glandulär-cystischen Hyperplasie. *Arch. Gynaek., 177:* 460-472, 1950.

2425. Zeit, P. R.: Myomas during and after the menopause. *Amer. J. Obstet. Gynec., 58:* 153-158, 1949.

See also Nos. 2229, 2488, 2551, 2558, 2562, 2584, 2645, 2789.

VI. Gastro-Intestinal System

2426. Bacon, H. E., and T. F. Moran: Management of hemorrhoids. *G. P., 2:* (2), 59-60, 1950.

2427. Collins, D. D.: The grave prognosis of appendicitis in the aged. *Ann, west. Med. Surg., 2:* 1-13, 1949.

2428. Debray, C., and R. Fleury: Traitement ambulatorie des hémorroïdes par les injections sclérosantes de solution huileuse d'acide phénique. *Paris méd., 40:* 171-173, 1950.

2429. De Grailly, R., and D. Berge: Les aspects anatomo-cliniques et les données fonctionnelles d'exploration du foie chez les vieillards; leur importance pour la diététique et la thérapeutique. *Rev. foie, 9:* (2), 57-68, 1950.

2430. de Jonge, T. E.: Das Altern des Gebisses. *Paradentologie, 4:* 83-98, 1950.

2431. Gier, L. J., and J. A. White: Histological study of the duodenum of the white rat. *Trans. Kansas Acad. Sci., 50:* 318-319, 1947. Abstr: *B. A., 22:* No. 1386, 1948.

2432. Gustafson, G.: Age determination on teeth. *J. Amer. dent. Ass., 41:* 45-54, 1950.

2433. Handler, P., and R. H. Follis, Jr.: Influence of age on hepatic response to choline and cystine deficiency in the rat. *Proc. Soc. exp. Biol., N. Y., 75:* 567-570, 1950.

2434. Hodges, F. B., Jr.: The injection treatment of hemorrhoids. *J. med. Ass. Ga., 39:* 279-280, 1950.

2435. Loeb, M. J.: Intestinal obstruction at the extremes of life. *Amer. Practit., 3:* 227-230, 1948.

2436. Muratori, F.: La prova dell'acido ippurico nelle epatopatie croniche in corso di terapia lipotropa. *Minerva med., Torino, 41:* 1056-1057, 1950.

2437. Ryan, E. J.: The dental problems of senescence. *Amer. Practit., 1:* 703-705, 1950.

2438. Schepel, J. A. C.: Operatie van een 101-jarige voor een geperforeerde appendix. *Ned. Tijdschr. Geneesk., 94:* 1508-1510, 1950.

2439. Spang, K.: Das Altersulkus des Magens und Zwölffingerdarms; Klinik und Pathogenese. *Dtsch. med. Wschr., 72:* 605-608, 1947.

2440. Wynn-Williams, A.: The stomach of the recently deceased. *Brit. med. J., 1950:* 102-104, 1950. Abstr: *B. A., 24:* No. 17902, 1950.

See also Nos. 2243, 2775.

VII. Kidney

2441. de Gouvea, G. S.: Neoplasmas renais do adulto. *Rev. brasil. Cirurg., 19:* 391-434, 1950.

2442. Jaffe, H. L., A. M. Master, and W. Dorrance: The salt depletion syndrome following mercurial diuresis in elderly persons. *Amer. J. med. Sci., 220:* 60-65, 1950.

2443. Olbrich, O.: Renal function of the aged hypertensives and nephrosclerotics. *Rev. méd. Liège, 5:* 647-649, 1950.

2444. Prado Tagle, E., M. Plaza de los Reyes, J. Parga, R. Crux-Coke, and O. Gaete: Consideraciones sobre la depuración plasmática del tiosulfato de sodio en individuos normales. *Rev. méd. Chile, 78:* 239-244, 1950.

2445. Shock, N. W., D. F. Davies, R. K. McDonald, D. H. Solomon, J. H. Miller, and M. Landowne: Age changes in renal function. *Rev. méd. Liège, 5:* 649-651, 1950.

2446. Weissenborn, W.: Zur Frage der Nierenfunktionsprüfung vor der Prostatektomie. *Dtsch. med. Wschr., 75:* 855-857, 1950.

See also Nos. 2374, 2655, 2659.

IX. Muscular System

2447. Binet, L., F. Bourlière, and É. Florentin: Physiologie; l'effet de l'âge sur le tonus de repos du muscle strié chez l'homme. *C. R. Acad. Sci. U.R.S.S. (Dokl.), 231:* 393-395, 1950.

2448. Hertzberg, E. I., and R. L. Skomarovskaia: (Modifications of the skeletal muscular system in rheumatism.) *Arkh. pat., Moskva, 12:* 18-23, 1950.

2449. Ravet-Herion, —.: Étude des protéines musculaires et sériques de la souris en fonction de l'âge. *Rev. méd. Liège, 5:* 662-664, Oct. 1950.

See also No. 2553.

X. Nervous System
(neurology)

2450. André, M. J.: Un cas de sclérose latérale amyotrophique du vieillard. *Brux. méd., 30:* 1101-1104, 1950.

2451. Carroll, J.: The utilization of reinforcement techniques in the program for the hemiplegic. *Amer. J. occup. Ther., 4:* 211-213, 1950.

2452. Copp, S.: Gefässerweiternde Therapie cerebraler Gefässerkrankungen. *Mschr. Psychiat. Neurol., 117:* (4/5/6), 213-214, 1949. Abstr: *B. A., 24:* No. 18376, 1950.

2453. Edelman, I. S.: Paraplegia secondary to metastatic prostatic carcinoma treated with stilbestrol. Report of a case. *Ann. intern. Med., 31:* 1098-1102, 1949. Abstr: *B. A., 24:* No. 18386, 1950.

2454. Eiden, H. F., and H. Lechner: Über psychotische Zustandsbilder bei der Pickschen und Alzheimerschen Krankheit. *Arch. Psychiat. Nervenkr., 184:* 393-412, 1950.

2455. Krayenbühl, H.: Neurochirurgische Diagnostik und Therapie der Hemiplegie; ein Beitrag zur Indikationsstellung der zerebralen Arteriographie. *Dtsch. med. Wschr., 75:* 1177-1180, 1950.

2456. Lüers, T.: Über fronto-thalamische Syndrome bei der Pick'schen Krankheit. *Dtsch. Z. Nervenheilk., 164:* 179-198, 1950.

2457. Morel, F., and E. Wildi: Les noyaux hypothalamiques à la lumière de quelques processus histopathologiques, la lésion d'Alzheimer notamment. *Schweiz. Arch. Neurol. Psychait., 65:* 439-449, 1950.

2458. Newman, M. K., and L. Cohen: Physical medicine and rehabilitation in the management of hemiplegia in the adult. *J. Mich. med. Soc., 49:* 917-922, 1950.

2459. Rexed, B.: Contributions to the knowledge of the postnatal development of the peripheral nervous system in man. A study of the bases and scope of systematic investigations into the fibre size in peripheral nerves. *Acta Psychiat., Kbh., Suppl. 33:* 1-206, 1944.

2460. Roger, H., J. Paillas, J. Roger, and J. Tamalet: Grande hydrocephalie latente du vieillard chez une démente artérioscléreuse. *Rev. neurol., 82:* 437-438, 1950.

2461. Rusk, H. A.: The rehabilitation of the hemiplegic patient. *N. Engl. J. Med., 243:* 690-693, 1950.

2462. Yamshon, L. J.: Rehabilitation of patients with hemiplegia. *Calif. Medicine, 73:* 181-182, 1950.

See also Nos. 2198, 2803, 2806.

XI. Reactions of the Body as a Whole

(allergy, anoxia, anesthesia, anthropometry, drugs, exercise, immunity, sleep, and temperature regulation)

2463. Bourlière, F., and M. Gourévitch: Âge et vitesse de réparation des plaies expérimentales chez le rat. *C. R. Soc. Biol., Paris, 144:* 377-379, 1950.

2464. Brožek, J., and A. Keys: Limitations of the

"normal" body weight as a criterion of normality. *Science, 112:* 788, 1950.

2465. Brull, L.: Organization of an experiment on the influence of nutrition on senescence and on resistance against Koch bacillus in the mouse. *Rev. méd. Liège, 5:* 660-662, 1950.

2467. Decourt, J., and J. M. Doumic: Les variations morphologiques de l'homme normal. *Sem. Hôp. Paris, 26:* 2462-2465, 1950.

2468. Gini, C.: The distribution of stature is hypernormal. *Acta genet., Basel, 1:* 361-376, 1949-1950.

2469. Goldberg, H. S.: The study of the normal temperature of school children aged two to five years. *J. Amer. osteop. Ass., 49:* 461-462, 1950. Abstr: *B. A., 24:* No. 29656, 1950.

2470. Gould, W. L.: Obesity and hypertension; the importance of a safe compound to control appetite, report of a series of 100 cases. *N. C. med. J., 11:* 327-334, 1950.

2471. Hegemann, G.: Standardmethode zur Beurteilung des Wundverlaufes. *Arch. klin. Chir., 264:* 168-173, 1950.

2472. Kling, D. H.: Failure of antireticular cytotoxic serum in arthritis. *J. Lab. clin. Med., 33:* 1289-1296, 1948.

2473. Layani, F., A. Bengui, and V. May: Le sérum cytotoxique (sérum de Bogomoletz et sérum orthobiotique) dans le traitement des rhumatismes. *Rev. Rhumat., Paris, 17:* 359-364, 1950.

2474. Leclerc, M.: Le sérum antiréticulocytotoxique de Bogomoletz. *Ann. Pharm. fr., 8:* 502-506, 1950.

2475. Morant, G. M.: The heights of British people. *Biol. Human Affairs, 16:* 20-26, 1950.

2477. Schlossmann, H. A.: Arzneiwirkung und Alter. *Arch. exp. Path., Berl., 208:* (2-3), 219-221, 1949.

2478. Tawast-Rancken, S.: (On gymnastics of middle-aged and old women.) *Geron, 1:* 33-39, 1949.

See also Nos. 2194, 2196, 2236, 2375, 2387.

XII. Reproductive System

(ovaries, testis see Endocrine System)

2479. Ahumada, J. C., A. E. Nogues, and H. L. Guixa: Patología quirúrgica ginecológica de la vejez. *Día méd., 22:* 2567-2572, 1950.

2480. Caraven, J.: Réactivation menstruelle de l'uterus trente-sept ans et demi après la ménopause. *Gynéc. et. Obstét., 49:* 318-320, 1950.

2481. Coldefy, J. M.: Cure radicale des gros prolapsus génitaux; considérations sur 15 cas de colpo-hystérectomies vaginales avec adossement vessie-rectum. *Bull. Ass. Gyn. Obst. Fr., 2:* 296-299, 1950.

2482. Corbett, D. G., and E. W. Abrams: Bilateral carcinoma of the male breasts associated with prolonged stilbestrol therapy for carcinoma of the prostate. *J. Urol., 64:* 377-381, 1950.

2483. Frost, A. C. G.: A review of 500 elective operations for pelvic prolapse on women over the age of 60 years. *Amer. J. Obstet. Gynec., 60:* 489-495, 1950.

2484. Geitmann, W. F., J. E. Fitzgerald, and B. P. Zummo: Elderly primiparas. *Amer. J. Obstet. Gynec., 56:* 846-852, 1948.

2485. Hillemann, G.: Der Genitalprolaps in der Praxis. *Deut. Gesundhwes., 5:* 1046-1049, 1950.

2486. Hunter, J. W. A.: The modern treatment of genital prolapse. *Med. Pr., 224:* 139-142, 1950.

2487. King, W. G.: Treatment of far advanced carcinoma of the breast. *Arch. Surg., Chicago, 61:* 630-653, 1950.

2488. Klees, E., and H. G. Müller: Funktioneller Zusammenhang zwischen Hiluszellen des Ovars und seniler Hyperplasia mucosae uteri. *Geburt. & Frauenheilk., 10:* 446-453, 1950.

2489. Latiers, F.: (Labor in older primipara.) *Strasbourg-méd., 1:* 275-283, 1950.

2490. Lopes de Faria, J.: Uterine and vaginal changes in rats with avitaminosis E. II. Collagenous fibers content of the endometrium of normal rats at different ages. *Ann. N. Y. Acad. Sci., 52:* 121-124, 1949. Abstr: *B. A., 24:* No. 26290, 1950.

2491. Lush, J. L.: Changes in milk production with age and milking frequency. *J. Dairy Sci., 33:* 338-357, 1950. Abstr: *B. A., 24:* No. 23994, 1950.

2492. O'Sullivan, J. J.: Gynaecological problems of old age. *Practitioner, 165:* 141-147, 1950.

2493. Ravina, A., A. Sicard, Y. Pécher, C. Forès, B. Clavel, and J. Martineau: Metastases tardives et multiples d'un cancer du sein opéré; amélioration remarquable, mais temporaire, sous l'influence de fortes doses de propionate de téstosterone. *Bull. Soc. méd. Hôp. Paris, 66:* 977-981, 1950.

2494. Ricklin, P.: Zur Behandlung fortgeschrittner Mammakarzinome mit männlichem Sexualhormon. *Schweiz. med. Wschr., 80:* 902-906, 1950.

2495. Sadugor, M. G., and J. P. Palmer: Age, incidence, and distribution of 4,652 cases of carcinoma of the cervix. *Amer. J. Obstet. Gynec., 56:* 680-686, 1948.

2496. Taylor, S. G., III, D. P. Slaughter, W. Smejkal, E. F. Fowler, and F. W. Preston: The effect of sex hormones on advanced carcinoma of the breast. *Cancer, 1:* 604-617, 1948. Abstr: *B. A., 24:* No. 26676, 1950.

2497. Tyler, A., and E. Atkinson: Prolongation of the fertilizing capacity of sea-urchin sperma-

tozoa by amino acids. *Science, 112:* 783-785, 1950.

2498. van der Plassche, M., and F. Paredia: Hoe lang haudt stierensperma zijn bevruchtingskracht binnen het geslachtsapparaat van vrouwelijke runderen. *Tijdschr. Diergeneesk., 74:* 831-838, 1949. Abstr: *B. A., 24:* No. 17959, 1950.

2499. Vara, P.: Studien über alte Erstgebährende. *Acta obstet. gynec. scand., 26:* 1-133, 1946. Abstr: *B. A., 22:* No. 1826, 1948.

2500. Zuckermann, C., D. Ramirez, J. C. Graham, and H. Romo Bolan: Prolapso genital; problema terapéutico. *Arch. Méd. Mex., 8:* 276-279, 1950.

2501. Anonymous: Elderly primagravida. *Lancet, 256:* 696-697, 1949.

2502. Anonymous: Tratamiento del prolapso genital; criterio y experiencia regional. *Gin. & Obstet. México, 5:* 167-180, 1950.

See also Nos. 2413, 2415, 2714.

XIII. Respiratory System

2503. Bates, D. V., and R. V. Christie: Intrapulmonary mixing of helium in health and in emphysema. *Clin. Sci., 9:* 17-29, 1950. Abstr: *B. A., 24:* No. 23065, 1950.

2504. Bohn, W.: Über Altersveränderungen am Lungenhilus. *Virchows Arch., 318:* 289-308, 1950.

2505. Dempsey, N.: Drop in tuberculosis deaths among young people calls for increased emphasis in older age groups. *Bull. Nat. Tuberc. Ass., N. Y., 36:* 136-137, 1950.

2506. Gordon, B., H. L. Motley, P. A. Theodos, and L. P. Lang: Physiological aspects and treatment of emphysema. *Geriatrics, 5:* 303-309, 1950.

2507. Kotsovsky, D.: Abriss der Therapie des Respirationssystems im Alter. *Med. Mschr., 4:* 742-744, 1950.

2508. Lancaster, H. O.: Tuberculosis mortality in Australia; 1908 to 1945. *Med. J. Aust., 1:* 655-662, 1950.

2509. Livingstone, J. L.: Pulmonary disease in the elderly. *Practitioner, 165:* 124-127, 1950.

2510. Metrop. Life Insur. Co.: Current outlook for tuberculosis. *Statist. Bull. Metrop. Life Insur. Co., 31:* 1-4, Nov. 1950.

2511. Schechtmann, M. R.: Examen de la función respiratoria; indices volumétricos normales. *Día méd., 22:* 1842-1847, 1950.

2512. Tiffeneau, R., and P. Drutel: Emphysème pulmonaire; étude clinique, spirographique et bronchométrique. *Paris méd., 40:* 327-332, 1950.

2513. Townsend, J. G.: Investigation of smog incident in Donora, Pennsylvania and vicinity. *Amer. J. publ. Hlth., 40:* 183-189, 1950. Abstr: *B. A., 24:* No. 23827, 1950.

2514. Whitfield, A. G. W., J. A. H. Waterhouse, and W. M. Arnott: The total lung volume and its subdivisions; a study in physiological norms; basic data. *Brit. J. soc. Med., 4:* 1-25, 1950.

2515. Whitfield, A. G. W., J. A. H. Waterhouse, and W. M. Arnott: The total lung volume and its subdivisions; a study in physiological norms; the effect of posture. *Brit. J. soc. Med., 4:* 86-97, 1950.

XIV. Sense Organs and Perception

2516. Babel, J.: L'évolution histologique des psuedotumeurs maculaires séniles. *Ann. oculist., Paris, 181:* 613-620, 1948.

2517. Bechgaard, P., K. Porsaa, and H. Vogelius: Ophthalmological investigations of 500 persons with hypertension of long duration. *Brit. J. Ophthal., 34:* 409-424, 1950.

2518. Birren, J. E., and N. W. Shock: Age changes in rate and level of visual dark adaptation. *J. appl. Physiol., 2:* 407-411, 1950. Abstr: *B. A., 24:* No. 23346, 1950.

2519. Brückner, A.: Entoptische Altersphänomene. *Ophthalmologica, 120:* 38-41, 1950.

2520. Charalampous, F. C., and D. M. Hegsted: Effect of age and diet on development of cataracts in the diabetic rat. *Amer. J. Physiol., 161:* 540-544, 1950.

2521. Covell, L. L.: Presbyopia; comparative observations of white and negro populations. *Amer. J. Ophthal., 33:* 1275-1276, 1950.

2523. Doesschate, J., and F. P. Fischer: Pterygium en pinguecula als ouderdomsverschijnsel. *Ned. Tijdschr. Geneesk., 94:* 1332-1334, 1950

2524. Elwyn, H.: The problem of glaucoma. *Amer. J. Ophthal., 33:* 1373-1379, 1950.

2525. Friedenwald, J. S.: Some problems in the diagnosis and treatment of glaucoma. *Amer. J. Ophthal., 33:* 1523-1538, 1950.

2526. Joy, H. H.: *Nevus flammeus* associated with glaucoma. *Amer. J. Ophthal., 33:* 1401-1409, 1950.

2527. Kravitz, D.: Glaucoma; some social and medical aspects. *Amer. J. Ophthal., 33:* 1381-1387, 1950.

2528. Lemoine, A. N., Jr.: Glaucoma; a statistical review of 816 patients with 1,112 glaucomatous eyes. *Amer. J. Ophthal., 33:* 1353-1373, 1950.

2529. Leschke, F.: Die Behandlung der Altersschwerhörigkeit mittels Vitamin A. *Zschr. Laryng., 29:* 238-239, 1950.

2530. McCulloch, C.: Iridoschisis as a cause of

glaucoma. *Amer. J. Ophthal., 33:* 1398-1400, 1950.

2531. Orma, E.: (Aging and the functions of the sense organs.) *Geron., 1:* 46-54, 1949.

2532. Porta, C. F.: Dysharmonies vasculaires de l'oreille dans la sénilité. *Rev. méd. Liège, 5:* 644, 1950.

2533. Posner, A., and A. Schlossman: The visual field as an aid to prognosis in glaucoma. *Amer. J. Ophthal., 33:* 1391-1397, 1950.

2534. Redl, T.: Über eine Sippe mit teils präseniler, teils infantiler erblicher Katarakt. *Klin. Mbl. Augenheilk., 114:* 24-33, 1949.

2535. Rosengren, B.: Studies in depth of the anterior chamber of the eye in primary glaucoma. *Arch. Ophthal., Chicago, 44:* 523-538, 1950.

2536. Schlosshardt, H.: Rückbildung diabetischer Linsentrübungen im vorgeschrittenen Lebensalter. *Klin. Mbl. Augenheilk., 116:* 237-246, 1950.

2537. Vogelius, H., and P. Bechgaard: The ophthalmoscopical appearance of the fundus oculi in elderly persons with arteriosclerosis and normal blood pressures. *Brit. J. Ophthal., 34:* 404-408, 1950.

2538. Waardenburg, P. J.: Über das familiäre Vorkommen und den Erbgang des praesenilen und senilen Glaukoms. *Genetica, 25:* (1-2), 79-125, 1950.

2539. Weekers, R.: Quelques données quantitatives sur la sénescence du cristallin. *Rev. méd. Liège, 5:* 674-679, 1950.

2540. Wick, R. E.: Geriatrics and optometry. *Amer. J. Optom., 27:* 109-116, 1950. Abstr: *P. A., 24:* No. 5757, 1950.

2541. Wick, R. E.: Visual changes with age. *Amer. J. Optom., 27:* 179-186, 1950. Abstr: *P. A., 24:* No. 5758, 1950.

See also No. 2580.

XV. Skeletal System

2542. Decker, P., and J. D. Buffat: Les affections chroniques de la colonne vertébrale; arthroses et hernies discales. *Helv. chir. acta, 17:* 187-233, 1950.

2543. Walthard, K. M.: Traitements physiothérapique du rhumatisme de la colonne cervicale et des algies cervicobrachiales. *Méd. & Hyg., 8:* 192, 1950.

See also No. 2547.

XV-A. Skeletal System: *Bone*

2544. Beizer, L. H.: Aspiration biopsy of bone marrow in diagnosis of multiple myeloma. *Geriatrics, 5:* 314-320, 1950.

2545. Estridge, M. N.: Paget's disease and intracranial tumor; association of an astrocytoma of right temporal lobe with osteitis deformans. *Bull. Los Angeles neurol. Soc., 15:* 87-92, 1950.

2546. Hart, G. M.: Post-menopausal osteoporosis of the spine. *Geriatrics, 5:* 321-330, 1950.

2547. Pañella-Casas, M., and —. Monteys-Orta: La cyphose sénile ostéoporotique. *Rev. méd. Liège, 5:* 697-708, 1950.

2548. Quigley, T. B.: The management of simple fracture of the clavicle in adults. *New Engl. J. Med., 243:* 286-290, 1950.

2549. Rudy, R. L., and V. L. Tharp: Tibial fracture in an aged stallion. *J. Amer. vet. Med. Ass., 117:* 199-201, 1950.

2550. Seigman, E. L., and W. L. Kilby: Osteopetrosis; report of a case and review of recent literature. *Amer. J. Roentgenol., 63:* 865-874, 1950.

2551. Smith, P. H., and A. M. Richardson: Post-menopausal osteoporosis; its clinical features. *J. Amer. med. Ass., 116:* 2465, 1941.

See also No. 2229.

XV-E. Skeletal System: *Arthritis and Rheumatism*

2552. Antognetti, L.: Recenti acquisizioni in tema di reumatologia. *Arch. "E. Maragliano", 5:* 631-636, 1950.

2553. Bayer, H.: Die Bedeutung des mechanischen Faktors für die Entstehung des muskelrheumatischen Schmerzes. *Dtsch. med. Wschr., 75:* 854-855, 1950.

2554. Bayles, T. B.: Hypertrophic arthritis (degenerative joint disease). *Med. Clin. N. Amer., 34:* 1435-1446, 1950.

2555. Briquemont, M.: Rheumatisme et maladie d'Addison. *Scalpel, Brux., 103:* 494-496, 1950.

2556. Coste, F., F. Delbarre, M. Bourel, and G. Basset: Tests fonctionnels surrenaux dans les polyarthrites chroniques évolutives. *Rev. Rhumat., Paris, 17:* 201-210, 1950.

2557. de Sèze, S., and J. Durieu: Remarques et hypotheses sur le rôle des facteurs vasculaires dans la pathogénie des arthroses et de la coxarthrose en particulier. *Rev. Rhumat., Paris, 17:* 215-218, 1950.

2558. Dingemanse, E., —. Huis, and L. G. Veld: Excretion of certain neutral 17-ketosteroids after administration of corticotrophin to patients with chronic rheumatism. *Acta physiol. pharm. neerl., 1:* 313-322, 1950.

2559. Donald, H. R.: The endocrine approach to arthritis. *N. Z. med. J., 49:* (271), 195-205, 1950.

2560. Ensign, D. C., and J. W. Sigler: The hands in arthritis. *J. Mich. med. Soc., 49:* 1078-1080, 1950.

2561. Françon, F.: (Arthritis of the hip.) *Acta physiother. rheumat. belg., 5:* 5-49, 1950.

2562. Freund, H. A., D. H. Basinski, and R. B. Scott: 17-ketosteroid excretion in rheumatoid arthritis. *J. Mich. med. Soc., 49:* 1076-1077, 1950.

2563. Freund, H. A., and C. S. Stulberg: The hemagglutination test for rheumatoid arthritis. *J. Mich. med. Soc., 49:* 1084, 1950.

2564. Giraud, G., J-M. Bert, F. Boyer, and J. Mirouze: Association d'une nevraxite et d'une polyarthrite chronique évolutive. *Montpellier méd., 37-38,* 112-114, 1950.

2565. Gueguen, Y.: Trouble statiques et rhumatismes chroniques. *Médecin fr., 10:* 215-217, 1950.

2566. Herzmark, M. H.: Chronic arthritis in Reiter's syndrome; report of two cases. *Med. Ann. District of Columbia, 19:* 428-430, 1950.

2567. Ingelrans, P., and H. Oberthur: Les arthrites sacro-iliaques non tuberculeuses. *Paris méd., 40:* i-ii, 1950.

2568. Juchum, M.: Der Rheumatismus in seiner sozialpolitischen und sozialhygienischen Bedeutung. *Hippokrates, 21:* 263-267, 1950.

2569. Kelly, M.: The prevention of deformity in rheumatic disease. *Med. J. Aust., 2:* 1-8, 1950.

2570. Köhler, V., and L. Penew: Nebennierenrindenhormon und *Arthritis rheumatica. Arztl. Wschr., 5:* 302-304, 1950.

2571. Lansbury, J., W. R. Crosby, and C. T. Bello: Precipitin reaction of serum from cases of rheumatoid arthritis with homologous connective tissue extracts. *Amer. J. med. Sci., 220:* 414-417, 1950.

2572. Lightbody, J. J.: Arthritis research in Michigan. *J. Mich. med. Soc., 49:* 1042-1044, 1950.

2573. Louyot, P., M. Vérain, and —. Vidal: Les modifications de la chlorémie dans les affections rhumatismales. *Rev. Rhumat., Paris, 17:* 65-68, 1950.

2574. Pfeffer, K. H., and H. Staudinger: Ausscheidung von Nebennierenrindenhormon bei *Polyarthritis rheumatica. Klin. Wschr., 28:* 451, 1950.

2575. Pickering, G. W.: Significance of the discovery of the effects of cortisone on rheumatoid arthritis. *Lancet, 2:* 81-84, 1950.

2576. Quinn, R. W., and S. J. Liao: A comparative study of antihyaluronidase, antistreptolysin "O", antistreptokinase, and streptococcal agglutination titers in patients with rheumatic fever, acute hemolytic streptococcal infections, rheumatoid arthritis and non-rheumatoid forms of arthritis. *J. clin. Invest., 29:* 1156-1166, 1950.

2577. Ravault, P., G. Vignon, and L. Berthier: Aux confins de la maladie de Bouillaud; le rhumatisme articulaire subaigu de l'adulte. *Rev. Rhumat., Paris, 17:* 290-294, 1950.

2578. Regan, C., and K. Myer: Hyaluronic acid hyaluronidase and the rheumatic diseases. *Ann. N. Y. Acad. Sci., 52:* 1108-1111, 1950.

2579. Routh, J. I., and W. D. Paul: Electrophoretic analyses of plasma and serum proteins in rheumatoid arthritis. *Arch. phys. Med., 31:* 511-517, 1950.

2580. Rubens-Duval, A., and J. Wibrotte: Les composantes psychiques de la douleur dans les affections rhumatismales. *Concours méd., 72:* 2415-2418, 1950.

2581. Steck, I. E., M. M. Montgomery, C. I. Reed, and N. R. Joseph: Influence of adrenocorticotrophic hormone (ACTH) on differences of potential between synovial fluid and skin in rheumatoid arthritis. *J. appl. Physiol., 3:* 84-90, 1950.

2582. Sugarman, H., and D. M. Baltzan: Primary splenic neutropenia with rheumatoid arthritis. *Canad. med. Ass. J., 63:* 72-74, 1950.

2583. Svartz, N.: Agglutination with sensitized sheep cells in rheumatoid arthritis. *J. Amer. med. Women's Ass., 5:* 261-262, 1950.

2584. Tarnopolsky, S., E. Montuori, and M. Schere: Eliminación de 17-cetoesteroides en artritis reumática o reumatoidea. *Prensa méd. argent., 37:* 1723-1724, 1950.

2585. Uehlinger, E., K. Akert, and W. Pirozynski: Nebennierenrindenhormone und Gelenke. *Bull. schweiz. Acad. med. Wiss., 6:* 157-170, 1950.

2586. van der Meer, P.: Algemene beschouwingen over het wezen van arthrosis deformans. *Ned. Tijdschr. Geneesk., 94:* 1900-1901, 1950.

2587. Winsbury-White, H. P.: Rheumatism in relation to chronic genito-urinary infection. *Rheumatism, 6:* 137-139, 1950.

XV-E. Skeletal System: *Arthritis and Rheumatism Therapy*

2588. Adams, C. H., and R. L. Cecil: Gold therapy in early rheumatoid arthritis. *Ann. intern. Med., 33:* 163-173, 1950.

2589. Albeaux-Fernet, M.: Le traitement des polyarthrites par l'emploi d'une hormone surrénale; la cortisone et 'une hormone hypophysaire; la corticotrophine. *Gaz. méd. Fr., 57:* 377-378, 1950.

2590. Albeaux-Fernet, D., and —. Deribreux: Premiers résultats du traitement du rhumatisme chronique par l'association vitamine C— désoxycorticostérone en injections intraveineuses. *Bull. Soc. méd. Hôp. Paris, 24:* 497-501, 1950.

2591. Alcacer Aguilar, F.: Reumatismo articular crónico y estreptomicina. *Medicamenta, Madrid, 8:* 408-410, 1950.

2592. Ant, M.: Vitamin E in rheumatism and arthritis. *Rheumatism, 6:* 114-121, 1950.

2593. Ant, M., and E. Di Cyan: Vitamin E in rheumatic diseases. *Ann. N. Y. Acad. Sci., 52:* 374-379, 1949. Abstr: *B. A., 24:* No. 26253, 1950.

2594. Armas Cruz, R., and C. Lackington: Novocaíne intravenosa en artropatías. *Rev. méd. Chile, 78:* 529-532, 1950.

2595. Aschner, B.: Erfolgreiche Behandlung des nicht-infektiösen Gelenkrheumas; Konstitutionstherapie und Hautausleitungsmethoden. *Hippokrates, 21:* 452-458, 1950.

2597. Boland, E. W., and N. E. Headley: Management of rheumatoid arthritis with smaller (maintenance) doses of cortisone acetate. *J. Amer. med. Ass., 144:* 365-372, 1950.

2598. Clark, W. S.: The relation of "N", "S" and "salt" hormone effects to the manifestations of rheumatoid arthritis. *J. clin. Invest., 29:* 805, 1950.

2599. Coggeshall, H. C.: The treatment of arthritis. *J. Indiana med. Ass., 43:* 853-855, 1950.

2600. Cohen, A., J. Goldman, A. W. Dubbs, and T. J. McBride: A preliminary report of twenty patients treated with Δ 5 pregnenolone and remissions in rheumatoid arthritis following gold therapy. *J. Lancet, 70:* 264-265, 1950.

2601. Copeman, W. S. C., O. Savage, P. M. F. Bishop, E. C. Dodds, B. Gottlieb, J. H. H. Glyn, A. A. Henly, and A. E. Kellie: A study of cortisone and other steroids in rheumatoid arthritis. *Brit. med. J., 2:* 849,-855, 1950.

2602. Crain, D. C., L. H. Kyle, and M. Rubin: The modern treatment of rheumatoid arthritis. *Postgrad. Med., 8:* 228-232, 1950.

2603. Daubresse, E.: Les implantations de stilboestrol dans le traitement des rhumatismes. *Paris méd., 40:* 147-152, 1950.

2604. Deguillaume, R.: Salicylothérapie et vitamines dans les rhumatismes chroniques. *Gaz. méd. Fr., 57:* 417-418, 1950.

2605. Dufrenoy, J.: Traitement de l'arthritisme par des hormones extraites de dioscorea du Mexique. *Rev. Path. comp., 50:* 424, 1950.

2606. Engi, E.: Erfahrungen mit Sympathisan bei rheumatischen Erkrankungen. *Münch. med. Wschr., 92:* 779-782, 1950.

2607. Fähndrich, W. H., and J. Junkersdorf: Vergleichende Untersuchungen zur parenteralen Pyramidontherapie, unter besonderer Berücksichtigung des chronischen Gelenkrheumatismus. *Dtsch. med. Wschr., 75:* 1145-1148, 1950.

2608. Ferond, M.: Les stéroïdes autres que le cortisone dans l'arthrite rhumatoïde. *Scalpel, Brux., 103:* 851-853, 1950.

2609. Freeman, H., and G. Pincus: Oral steroid administration in rheumatoid arthritis. *J. clin. Endocrinol., 10:* 824, 1950.

2610. Freyberg, R. H.: The use of cortisone and ACTH in rheumatoid arthritis. *Bull. rheumat. Dis., 1:* 1-2, 1950.

2611. Gilbert, J. T., Jr., and F. H. Moore: Gold therapy in rheumatoid arthritis. *J. Ky. med. Ass., 48:* 308-314, 1950.

2612. Godlowski, Z. Z.: Stimulation of the suprarenal glands in the treatment of rheumatoid arthritis. *Ann. rheumat. Dis., 8:* 285, 1949. Abstr: *B. A., 24:* No. 23153, 1950.

2613. Gorsuch, M. T.: Clinical and laboratory investigation of sodium gentisate as an anti-rheumatic treatment. *Med. Wom. J., 57:* (9), 9-23, 1950.

2614. Goslings, J., W. Hijmans, and P. M. van Limpt: Clinical administration of corticotropic hormone in the therapy of rheumatoid arthritis. *J. clin. Endocrinol., 10:* 797-799, 1950. Also *in: Ned. Tijdschr. Geneesk., 94:* 2243-2254, 1950.

2615. Graham, W., T. E. Hunt, and D. Mowat: Rheumatoid arthritis; results of treatment with desoxycorticosterone acetate and ascorbic acid (arthrodox). *Canad. med. Ass. J., 63:* 121-123, 1950.

2616. Grivaux, M.: L'action de la Δ-5-pregnenolone dans la polyarthrite évolutive. *Sem. Hôp. Paris, 26:* 2298-2299, 1950.

2617. Haydu, G. G.: Studies on the pathogenesis of rheumatoid arthritis; clinical observations during and after a course of insulin and simultaneous administration of glucose and glucose metabolities to patients with rheumatoid arthritis. *Rheumatism, 6:* 133-136, 1950.

2618. Henderson, E., J. W. Gray, M. Weinberg, E. Z. Merrick, and H. Seneca: Some preliminary observations on the treatment of rheumatoid arthritis with cortisone plus insulin. *J. clin. Endocrinol., 10:* 800-801, 1950.

2619. Holbrook, W. P., D. F. Hill, C. A. L. Stephens, Jr., and L. J. Kent: Effects of ACTH and cortisone on rheumatoid arthritis. *Arizona Med., 7:* 43-44, 1950.

2620. Jonsson, E., K. Berglund, E. Y. Hakanson, N. G. Hävermark, and H. Laurell: Biochemical and clinical studies in rheumatoid arthritis during administration of adrenocorticotrophic hormone (ACTH). *Acta endocr., Kbh., 4:* 229-239, 1950.

2621. Justin-Besançon, L.: La crénotherapie des rhumatismes chroniques. *Sem. Hôp. Paris, 26:* 2669-2676, 1950.

2622. Kempf, W.: Die parenterale Goldbehandlung

des chronischen Gelenkrheumatismus. *Dtsch. med. Wschr., 75:* 1037-1039, 1950.

2623. Kersley, G. D., L. Mandel, M. R. Jeffrey, M. H. L. Desmarais, and E. Bene: Insulin and E.C.T. in treatment of rheumatoid arthritis; report on a pilot series of cases. *Brit. med. J., 2:* 855-860, 1950.

2624. Kling, D. H.: Treatment of rheumatoid arthritis with progesterone and pregnenolone. *Ann. west. Med. Surg., 4:* 378-382, 1950.

2625. Kuhns, J. G., and T. A. Potter: Nylon arthroplasty of the knee joint in chronic arthritis. *Surg., Gynec. Obstet., 91:* 351-362, 1950.

2626. La Vay, D.: The place of orthopaedic surgery in the treatment of chronic rheumatic conditions of the hip and knee joints. *Rheumatism, 6:* 99-113, 1950.

2627. Lightbody, J. J., A. E. Price, W. S. Reveno, and E. C. Voderheilde: Cortisone in rheumatoid arthritis; observations of 15 patients. *J. Mich. med. Soc., 49:* 1085-1088, 1950.

2628. Lipkin, E.: Procaine in rheumatic diseases. *J. Mich. med. Soc., 49:* 1081-1083, 1950.

2629. Loxton, G.: Recent advances in the treatment of rheumatoid arthritis. *Post Grad. med. J., 26:* 447-451, 1950.

2630. Luft, R., B. Sjogren, and C. H. Li: The effect of small dosages of ACTH protein and ACTH peptides in cases of rheumatoid arthritis. *J. clin. Endocrinol., 10:* 823-824, 1950.

2631. Meyer, K., and C. Ragan: L'action antirhumatismale du gentisate de sodium. *Rev. gén. méd. chir. Union fr., Alger, 27:* 1589, 1950.

2632. Moss, L.: The treatment of chronic rheumatism by the use of adrenalin cream. *Med. World, Lond., 72:* 486-491, 1950.

2633. Nyström, G.: Attempts to reproduce the effects of ACTH or of compound E in rheumatoid arthritis by means of other hormones and steroids. *Acta endocr., Kbh., 4:* 240-264, 1950.

2634. Pape, R.: Über indirekte Röntgenbestrahlungen bei Arthritis, Neuralgien und anderen Leiden. *Wien. med. Wschr., 100:* 332-336, 1950.

2635. Pellet, C.: Le traitement des rhumatismes diathésiques par le déhydrocholate de soude. *Rev. Rhumat., Paris, 17:* 316, 1950.

2636. Perera, G. A., and C. M. Plotz: The response to methacholine in rheumatoid arthritis. *Amer. J. med. Sci., 220:* 307-309, 1950.

2637. Polley, H. F., and H. L. Mason: Rheumatoid arthritis; effects of certain steroids other than cortisone and of some adrenal cortex extracts. *J. Amer. med. Ass., 143:* 1474-1481, 1950.

2638. Pompen, A. W. M.: Clinical experiences with adrenocorticotropic hormone (cortrophin) in a patient with chronic rheumatoid arthritis and in a patient with Sheehan's syndrome. *J. clin. Endocrinol., 10:* 794-795, 1950.

2639. Quin, C. E., R. M. Mason, and J. Knowelden: Clinical assessment of rapidly acting agents in rheumatoid arthritis. *Brit. med. J., 2:* 810-813, 1950.

2640. Roderfeld, —.: Praktische Erfahrungen über die Behandlung von Arthrosen und Polyarthritis mit dem Mistelpräparat Plenosol. *Deut. Gesundhwes., 5:* 953-954, 1950.

2641. Sladen, F. J.: Cortisone and ACTH; their present relationship to rheumatoid arthritis. *J. Mich. med. Soc., 49:* 1053-1057, 1950.

2642. Slocumb, C. H., H. F. Polley, P. S. Hench, and E. C. Kendall: Effects of cortisone and ACTH on patients with rheumatoid arthritis. *Proc. Mayo Clin., 25:* 476-478, 1950.

2643. Stock, J. P. P., and E. C. McClure: Pregnenolone in the treatment of rheumatoid arthritis. *Lancet, 2:* 125-128, 1950.

2644. Strazza, J. A., Jr.: Treatment of rheumatoid arthritis with pregnenolone. *J. med. Soc. N. J., 47:* 472-475, 1950.

2645. Terry, L. L., and F. London: Effects of Reichstein's compound S, pregnenetriolone acetate, and 17-alpha hydroxyprogesterone in rheumatoid arthritis. *Proc. Soc. exp. Biol., N. Y., 73:* 251-252, 1950. Abstr: *B. A., 24:* No. 23172, 1950.

2646. Trivelli, L.: L'ultrasuonoterapia nelle artrosi. *Arch. Ortop., 63:* 164-166, 1950.

2647. Tyson, T. L., H. H. Holmes, and C. Ragan: Copper therapy of rheumatoid arthritis. *Amer. J. med. Sci., 220:* 418-420, 1950.

2648. Wheatley, D.: Rheumatoid arthritis treated with anterior pituitary growth hormone. *Brit. med. J., 2:* 1472, 1950.

2649. Witzgall, J.: Die Behandlung der Gelenkerkrankungen mit NNR-Hormonen, mit einem vorläufigen Bericht über die kombinierte Anwendung von Desoxycorticosteronacetat und *l*-Ascorbinsäure. *Ther. Gegenw., 89:* 120-128, 1950.

2650. Wolfson, W. Q., H. D. Hunt, C. Cohn, W. Robinson, and I. F. Duff: ACTH and colchicine in the clinical treatment of acute gouty arthritis; physiological considerations and review of therapeutic results in 51 attacks. *J. Mich. med. Soc., 49:* 1058-1064, 1950.

2651. Wramner, T.: Studies on the effect of neostigmine on muscular symptoms in rheumatoid arthritis. *Acta med. scand., Suppl. 242,* 1-59, 1950.

2652. Zinn, W., and V. Sonnenschein: Ergebnisse der Ultraschalltherapie rheumatischer und degenerativer Gelenkerkrankungen; eine neural-

pathologische Studie. *Dtsch. med. Wschr., 75:* 827-830, 1950.

2653. Anonymous: Present status of percorten and ascorbic acid in rheumatoid arthritis. *Ciba clin. Symposia, 2:* (Suppl.), 1-8, Dec. 1950.

See also Nos. 2310, 2318, 2400, 2402, 2448, 2473, 2744.

XV-E. Skeletal System: *Gout*

2654. Benedict, J. D., P. H. Forsham, M. Roche, S. Soloway, and D. Stetten, Jr.: The effect of salicylates and adrenocorticotropic hormone upon the miscible pool of uric acid in gout. *J. clin. Invest., 29:* 1104-1111, 1950.

2655. Brown, J., and G. K. Mallory: Renal changes in gout. *New Engl. J. Med., 243:* 325-329, 1950.

2656. Favarger, P.: Étude chimique de trois cas de goutte lipidique dont deux cas familiaux et un apparemment sporadique. *Arch. int. Pharmacodyn., 68:* 81-94, 1942. Abstr: *B. A., 24:* No. 29374, 1950.

2657. Françon, F.: La main dans la goutte. *Rhumatologie,* No. 3, 91-98, May-June 1950.

2658. Françon, F.: Pathogénie de la goutte. *Un. méd. Can., 79:* 1173-1176, 1950.

2659. Friedman, M., and S. O. Byers: Increased renal excretion of urate in young patients with gout. *Amer. J. Med., 9:* 31-34, 1950.

2660. Gutman, A. B., and T. F. Yü: Effects of adrenocorticotropic hormone (ACTH) in gout. *Amer. J. Med., 9:* 24-30, 1950.

2661. Leopold, H. N.: ACTH and colchicine in therapy of gout; report of a case of acute gouty arthritis. *Texas St. J. Med., 46:* 710-712, 1950.

2662. Örström, Å, and M. Örström: The role of glutamine in metabolism, with special regard to the formation of uric acid in gout. *Acta med. scand., 138:* 108-120, 1950.

2663. Parturier, G., and M. Faures: Contribution à la pathogénie des crises de goutte. *Rev. méd. chir. mal. foie, 25:* (5), 29-30, 1950. Also *in: Bull. Soc. méd. Hôp. Paris, 66:* 952-953, 1950.

2664. Talbott, J. H., and L. M. Lockie: Gouty arthritis. *Ciba clin. Symp., 2:* (10), 319-340, 1950.

2665. Vignes, H.: À propos de la goutte. *J. Prat., Paris, 64:* 336-339, 1950.

2666. Vignon, G.: Les arthropathies goutteuses; aspects cliniques et traitement. *Médecin fr., 10:* 211-213, 1950.

2667. Wolfson, W. Q., C. Cohn, W. Wise, and S. Sideman: Administration and subsequent withdrawal of ACTH, studied simultaneously in a gouty father and his hyperuremic son. *J. clin. Endocrinol., 10:* 835, 1950.

See also No. 2420.

XVI. Skin and Integument

2669. Boileau, Y.: Influences hormonales sur la vitalité de la pousse des cheveux. *J. Prat., Paris, 64: 277-278,* 1950.

2670. Cawley, E. P., and A. C. Curtis: Lentigo senilis. *Arch. Derm. Syph., N. Y., 62:* 635-641, 1950.

2671. de Graciansky, P., A. Carteaud, and S. Boulle: Quelques alopécies rares. *Sem. Hôp. Paris, 26:* 2108-2112, 1950.

2672. Ferrucci, M.: L'alopecia areata e le infezioni focali dentarie; considerazioni su caso clinico. *Dermosifilografo, 25:* 317-323, 1950.

2673. Geiringer, E.: Vitamin C and achromotrichia. *Rev. méd. Liège, 5:* 664-667, 1950.

2674. Goldzieher, J. W., W. B. Rawls, I. S. Roberts, and M. A. Goldzieher: The effect of steroid hormones applied directly to senile human skin. *J. clin. Endocrinol., 10:* 831-832, 1950.

2675. Grant, R., T. Cornbleet, and M. I. Grossman: Influence of local application of adrenal cortical extract on hair growth in the human. *Arch. Derm. Syph., N. Y., 62:* 717-718, 1950.

2676. Hall, A. F.: Treatment of senile keratoses with podophyllin. *Arch. Derm. Syph., N. Y., 62:* 362-369, 1950.

2677. Hoffmann, G. R.: La thermométrie cutanée chez le sujet normal. *Acta clin. belg., 5:* 241-249, 1950.

2678. Kennedy, R. J.: The treatment of pruritus with adenosine-5-monophosphate (muscle adenylic acid). *N. Y. St. J. Med., 50:* 1609-1610, 1950.

2679. Khodkov, V. N.: (Treatment of chronic ulcers in the leg.) *Med. Sestra, Moskva,* No. 8, 21-24, Aug. 1950.

2680. Kohen, I.: Traitement des ulcères de jambe par le sérum orthobiotique. *Bull. Soc. franc. Derm. Syph., 57:* 176-177, 1950.

2681. Lowenfish, F. P.: Treatment of *pruritus ani, vulvae et scroti. J. Lancet, 70:* 266, 1950.

2682. Midana, A., and M. Dogliotti: La tubocurarina nel trattamento dei pruriti "essenziali". *Dermosifilografo, 25:* 179-185, 1950.

2683. Simon, C., and P. Fouquet: Pelade décalvante totale, en voie de guérison chez un obsédé, traité par psychothérapie. *Bull. Soc. franc. Derm. Syph., 57:* 189-191, 1950.

2684. Thomson, S.: Skin disorders in the elderly. *Practitioner, 165:* 128-134, 1950.

2685. Trotter, M., and O. H. Duggins: Age changes in head hair from birth to maturity. I. Index and size of hair of children. *Amer. J. phys. Anthrop., 6:* 489-506, 1948.

2686. Tunbridge, R. E., W. T. Astbury, R. N. Tattersall, R. Reed, G. Eaves, and D. A. Hall:

Observations on the nature of the changes in senile skin. *Rev. méd. Liège, 5:* 671-674, 1950.

2687. Wirth, L.: Evaluation of oral priscoline as an antipruritic agent. *Milit. Surg., 107:* 131, 1950.

2688. Anonymous: Cause of common baldness; the scalp tension theory. *What's New, Chicago,* No. 148, 2-4, July-Aug. 1950.

2689. Anonymous: De l'alopécie. *J. Prat., Paris, 64:* 89-90, 1950.

See also Nos. 2386, 2405.

XVII. Urogenital System (prostate)

2690. Albeaux-Fernet, M.: Le cancer de la prostate; problèmes actuels de sa thérapeutique. *J. Prat., Paris, 64:* 185-187, 1950.

2691. Andersen, P. E.: Estrogen therapy in prostatic carcinoma. *Acta radiol., Stockh., 34:* 33-46, 1950.

2692. Andrews, B. W., and J. W. Barry: Female prostatism. *Urol. cutan. Rev., 54:* 269-271, 1950.

2693. Balogh, F., L. Zádor, and D. Vecsey: (Cytologic examination of prostatic secretion in tumors of the latter.) *Magyar Sebészet, 3:* 239-241, 1950.

2694. Bottou, M.: A propos du traitement des cancers de la prostate. *Maroc méd., 29:* 653-655, 1950.

2695. Brendler, H., W. E. Chase, and W. W. Scott: Prostatic cancer; further investigation of hormonal relationships. *Arch. Surg., Chicago, 61:* 433-440, 1950.

2696. Carson, R. B.: Leiomyoma of the prostate; case report. *J. Urol., 64:* 373-376, 1950.

2697. Colston, J. A. C.: Carcinoma of the prostate. *G. P., 2:* (4), 53-57, 1950.

2698. Connor, J. J., S. Heinemann, and J. M. Machish: Prostatism complicated by chronic lymphatic leukemia. *Urol. cutan. Rev., 54:* 276-279, 1950.

2699. Couvelaire, R.: Qu'est-ce qu'un "prostatique" et comment l'examiner? *Pr. méd., 58:* 744-745, 1950.

2700. de Castro Barbosa, N.: Contribuiçaò ao tratamento do câncer da próstata. *Rev. brasil. Med. Pharm., 7:* 248-251, 1950.

2701. de Faria, G.: Diagnóstico diferencial entre hipertrofia benigna e câncer da próstata. *Rev. brasil. Med. Pharm., 7:* 413-416, 1950.

2702. Detrie, P.: Le diagnostic cytologique du cancer de la prostate. *Pr. méd., 58:* 876, 1950.

2703. Gilbert, G. C.: Operative results in prostatic surgery. *N. C. med. J., 11:* 341-344, 1950.

2704. Greco, G.: Determinazione delle fosfatasi acida e alcalina nel siero di sangue per la diagnosi del carcinoma della prostata. *G. ital. Chir., 6:* 484-495, 1950.

2705. Groen, J.: Treatment of carcinoma of the prostate with metastases in the bones by oestrogenic substances. *Acta brev. neerl. Physiol., 16:* 80, 1948. Abstr: *B. A., 24:* No. 26654, 1950.

2706. Hennig, O.: Das Wesen des Prostataleidens unter besonderer Berücksichtigung der nephrogenen Azidose. *Z. Urol., 43:* 304-320, 1950.

2707. Herrold, R. D.: Management of prostatitis. *Postgrad. Med., 8:* 237-239, 1950.

2708. Hertkens, H. J.: Erfahrungsbericht über 49 mit Cyren A behandelte Prostatakarzinome. *Z. Urol., 43:* 325-328, 1950.

2709. Huggins, C. B.: The effects of steroids on prostatic cancer. *In:* E. S. Gordon, (Editor), *A Symposium on Steroid Hormones,* Univ. Wis. Press, Madison, 1950, pp. 228-230.

2710. Jadassohn, W.: Las prostatitis, vesiculitis, epidimitis y orquitis no tuberculosas. *Arch. esp Urol., 6:* 280-290, 1950.

2711. Jönsson, G., and C. M. Fajers: Cancer cells in prostatic secretion. *Acta chir. scand., 99:* 545-559, 1950.

2712. Kawaichi, G. K., and P. Cooper: Leiomyosarcoma of the prostate; a case report. *Urol cutan. Rev., 54:* 399-401, 1950.

2713. Korpassy, B.: Vergleichende Untersuchungen über die Vorsteherdrüse von menschlichen Neugeborenen, Hunden und Katzenjungen. *Berl. u. münch. tierärztl. Wschr., 1943:* (37/38), 320-321, 1943. Abstr: *B. A., 24:* No. 29757, 1950.

2714. Linder, F.: Die Behandlung des Prostata- und Mammakrebses. *Ärztl. Wschr., 5:* 317-321, 1950.

2715. Mandl, K.: Prostatakarzinom-Behandlung mit Depot-Ostrogen. *Wien. med. Wschr., 100:* 438-439, 1950.

2716. Miller, C. O., M. R. Buehrig, and R. R. Haeger: A study of carcinoma of the prostate before and after advent of hormonal therapy. *Urol. cutan. Rev., 54:* 465-468, 1950.

2717. Mitchell, L., and J. R. Nixon: Sarcoma of the prostate. *Alberta med. Bull., 15:* 26-27, 1950.

2718. Neckels, —.: Multiple Blasensteine bei Prostatahypertrophie. *Z. Urol., 43:* 260, 1950.

2719. Nesbit, R. M., and W. C. Baum: Endocrine control of prostatic carcinoma; clinical and statistical survey of 1,818 cases. *J. Amer. med. Ass., 143:* 1317-1320, 1950.

2720. Nikolowski, W.: Über Abwegigkeiten der Prostatasekretion bei Prostatorrhöe. *Z. Urol., 43:* 233-236, 1950.

2721. Raines, S. L., and H. B. Maddux: Sarcoma

of the prostate; a review of the literature and case report. *Urol. cutan. Rev., 54:* 283-287, 1950.

2722. Renolds, L. R., T. L. Schulte, and H. J. Hammer: Carcinoma of the prostate gland; results of conservation management. *Arch. Surg., Chicago, 61:* 441-448, 1950.

2723. Schenker, J.: Zur functionellen Anatomie der Prostata des Rindes. *Acta anat., Basel, 9:* 89-102, 1950. Abstr: *B. A., 24:* No. 23301, 1950.

2724. Scher, S.: Some observations on the anatomy of the bladder neck and posterior urethra with reference to prostatic obstruction. *Brit. J. Urol., 22:* 116-124, 1950.

2725. Teilum, G.: Oestrogen production by Sertoli cells in the etiology of benign senile hypertrophy of the human prostate; testicular lipoid cell ratio and oestrogen-androgen quotient in human male. *Acta endocrinol., 4:* 43-62, 1950.

2726. Thumann, R. C., Jr., and D. Randall: Cystourethrography in the diagnosis of diseases of the prostatic urethra. *Amer. J. Roentgenol., 64:* 640-648, 1950.

2727. Trivedi, B. P.: Senile enlargement of prostate; pathological aspect. *J. Indiana med. Ass., 19:* 333-334, 1950.

2728. Trunnell, J. B., B. J. Duffy, Jr., V. Marshall, W. Whitmore, and H. Q. Woodard: The use of progesterone in treatment of cancer of the prostate. *J. clin. Endocrinol., 10:* 808, 1950.

2729. Turner, A. F., Jr.: The general practitioner's care of the prostate. *J. Fla. med. Ass., 37:* 27-30, 1950.

2730. Von Novak, E.: Hypertrophy of the prostate. *Indian med. J., 44:* 79-84, 1950.

2731. Waelsch, J. H., and J. Wolf: (Case of chronic lymphatic leukemia with hypertrophic prostate and its therapy with urethane.) *Čas. Lék. čes., 89:* 767-769, 1950.

2732. Whitfield, H. J.: Prostatism in the negro with clinical and pathological studies. *J. Urol., 64:* 106-113, 1950.

2733. Winsbury-White, H. P.: Genito-urinary disturbances in old age. *Practitioner, 165:* 135-140, 1950.

See also Nos. 2237, 2446, 2453, 2482.

GERIATRICS

I. General Orientation

2734. Boyd, D. A., Jr., and F. J. Braceland: The practitioner and the older age groups; psychosomatic aspects. *Med. Clin. N. Amer., 34:* 1091-1105, 1950.

2735. Desmond, T. C.: Promise of geriatrics. *Today's Hlth., 28:* 22-23, June 1950.

2736. Lavalée, G.: La gériatrie. *Concours méd., 72:* 2045-2046, 1950.

2737. Long, E. R.: Medical sciences and the longer life. *Diplomate, 20:* 199-203, 1948.

2738. Mars, G., and M. Morpurgo: Problemi di geriatria. *Osped. maggiore, 38:* 260-262, 1950.

2739. Sleeswijk, J. G.: De betekenis der gerontologie. *Ned Tijdschr. Geneesk., 94:* 2040-2042, 1950.

2740. T(hewlis), M. W.: A geriatric board. (Editorial). *Geriatrics, 4:* 194-195, 1949.

2741. Anonymous: Old people; well or sick. *Nurs. Mirror, 91:* 2-3, 1950.

See also No. 2187.

II. and III. Medical Care and Diagnosis

2742. Cherkasky, M.: The Montefiore hospital, home care program. *Amer. J. publ. Hlth., 39:* 163, 1949.

2743. Deardorff, N. R.: The 1948 experience of the health insurance plan of greater New York with the utilization of physician services by the enrollees in each age-sex group. *Amer. J. publ. Hlth., 40:* 1536-1545, 1950.

2744. Erickson, D. J.: Physical medicine for the home-bound arthritic. *Brit. J. phys. Med., 13:* 193-197, 1950.

2745. MacDonald, W.: Cues for handling elderly patients. *Med. Econ., 25:* 103, 1948.

2746. Newton, K.: *Geriatric nursing.* C. V. Mosby Co., St. Louis, 1950, 420 pp.

2747. Semple, A. B.: The care of the aged. *Nurs. Mirror, 91:* 341-342, 1950.

2748. Sleeswijk, J. G.: *(La vieillesse considérée du point de vue médical.)* Envers, Amsterdam, 2 vols, pp. 276 & 802, 1950.

2749. Sleeswijk, J. G.: La physiothérapie dans les maladies cardiovascularies des vieillards. Rev. *méd. Liège, 5:* 644-646, 1950.

2750. Thewlis, M. W., and E. T. Gale: Ambulatory care of the aged. *Geriatrics, 5:* 331-336, 1950.

2751. Vermillion, J. R.: New 87-bed chronic disease hospital in San Francisco. *Hosp. Mgmt., 70:* 4, 1950.

2752. Warren, M. W.: The facilities available for the care of the elderly in the home. *Practitioner, 165:* (986), 156-163, 1950.

2753. Watkins, A. L.: Current problems in physical medicine and rehabilitation. *New Engl. J. Med., 234:* 489-497, 1950.

2754. Anonymous: Hospital gives home care. *Hosp. Mgmt., 70:* 36-37, 1950.

2755. Anonymous: *Report on second informal midwestern conference of nursing homes, January 12-13, 1949.* Indiana Ass. Licensed Nursing Homes, Mid-Western Conf. of Nursing Homes, Indianapolis, 1949, 63 pp.

See also Nos. 2761, 3017, 3022.

IV. Disease

(chronic, infectious, and mental)

2756. Austregesilo, A.: Myéloses séniles. *Rev. neurol., 80:* 683-686, 1948.

2757. Bridgers, W. H., and R. B. Stith: Modern management of certain chronic diseases of middle life. *J. S. C. med. Ass., 44:* 381-390, 1948.

2758. Cahen-Salabelle, R.: La psychothérapie de la deuxième moitié de la vie d'après C. H. Jung. *Sem. Hôp. Paris, 26:* 2291-2293, 1950.

2759. Chervinskii, I. A.: (Age characteristics in the course of malarial infection in different age groups.) *Pediatriya,* No. 4, 3-8, July-Aug. 1950.

2760. Commission on Chronic Illness: *Proceedings of first meeting, Friday, May 20, 1949.* The Commission, Chicago, 1949, 73 pp.

2761. Covalt, N. K.: Physical medicine and rehabilitation study; one year report in particular relation to the chronically ill. *J. Amer. med. Ass., 144:* 1249-1255, 1950.

2762. Dejardin, J.: Étude statistique de l'invalidité dans l'assurance maladie-invalidité en Belgique. *Arch. Méd. sociale, Paris, 6:* 122-155, 1950.

2763. Firket, J., and M. Damiean-Gillet: Cancers au début de l'existence et fréquence relative des sarcomes suivant l'âge. *Rev. méd. Liège, 5:* 723-728, 1950.

2764. Fischer, W.: Über die bösartigen Geschwülste im hohen Alter. *Z. ges. innere Med., 2:* 119-122, 1947. Abstr: *B. A., 24:* No. 26997, 1950.

2765. Getting, V. A.: A coordinated state program for chronic illness. *Amer. J. publ. Hlth., 40:* 1251-1256, 1950.

2766. Granick, S.: Studies of psychopathology in later maturity; a review. *J. Geront., 5:* 361-369, 1950.

2767. Jervis, G. A.: Early senile dementia in mongoloid idiocy. *Amer. J. Psychiat., 105:* 102-106, 1948. Abstr: *B. A., 24:* No. 18439, 1950.

2768. Levin, M. L.: The chronic illness commission; its relation to industrial medicine. *Arch. industr. Hyg. & occup. Med., 2:* 9-11, 1950.

2769. Levin, M. L.: National planning for chronic disease control. *Publ. Aid Ill., 17:* 4-7; 11, Oct. 1950.

2770. Liebman, S., and R. L. French: Patient population distribution in mental hospitals in the United States. *Amer. J. Psychiat., 105:* 489-493, 1949.

2771. Lowe, C. R.: The care of the chronic sick. V. Investigation of 393 patients seeking admission to a hospital for the chronic sick. *Brit. med. J., 2:* 699-702, 1950.

2772. Mayo, L. W.: The National Commission on Chronic Illness. *Publ. Aid. Ill., 17:* 8-10, Oct. 1950.

2773. Moore, M. E., and B. S. Sanders: Extent of total disability in the United States. *Soc. Sec. Bull., 13:* 7-14, Nov. 1950.

2774. Orthner, F.: Zusammenhänge zwischen Alters- und Krebsproblem. *Wien. med. Wschr., 100:* 347-348, 1950.

2775. Ravault, P. P., H. Fraisse, and C. Loisy: La péritonite tuberculeuse du vieillard. *J. Méd. Lyon, 31:* 453-456, 1950.

2776. Reimer, M. D.: A study of the mental status of schizophrenics hospitalized for over 25 years into their senium. *Psychiat. Quart., 24:* 309-313, 1950.

2777. Robinson, C. B.: The problem of the aged in mental hospitals. *Ulster med. J., 19:* 5-11, 1950.

2778. Saslow, G.: The emotional problems of the chronically ill. *Minn. Med., 33:* 673-682, 1950.

2779. Shoor, M., and F. H. Adams: The intensive electric shock therapy of chronic disturbed psychotic patients. *Amer. J. Psychiat., 107:* 279-282, 1950.

2780. Slover, W. P.: The aged find a haven in "the annex". *Mod. Hosp., 71:* (6), 65-67, 1948.

2781. Wilczkowski, E.: (Pathophysiology of mental disorders of the involution period.) *Polsk. Tygod. lek., 4:* 65-70, 1949. Abstr: *B. A., 24:* No. 23128, 1950.

See also Nos. 2197, 2412, 2568, 2751, 2788, 2924.

V. Hygiene

2782. Clow, H. E.: Psychiatric factors in the rehabilitation of the aging. *Ment. Hyg., N. Y., 34:* 592-599, 1950.

2783. Drake, F., and K. Drake: How to live longer. *Amer. Mercury, 68:* 340-344, 1949. Also *in: Reader's Dig., 54:* 69-72, March 1949.

2784. Gruenberg, S. M.: Turbulent middle years. *Survey, 86:* 121-125, March 1950.

2785. Helfer, H.: How to live 100 years. *N. Y. Times Mag.,* Oct. 10, 1948, p. 64.

2786. Hershey, B.: Baruch plan for youth at 80. *N. Y. Times Mag.,* Aug. 13, 1950, p. 18.

2787. Jalavisto, E.: (Hygiene of the approaching old age.) *Geron, 1:* 55-61, 1949.

2788. Kaplan, O. J.: The mental health of older workers. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 204-218.

2789. Korenchevsky, V.: Rejuvenative, or preventive and eliminative treatment of senility. *Geriatrics, 5:* 297-302, 1950.

2790. Tenny, A. S.: How to live longer; reply with rejoinder. *Amer. Mercury, 68:* 766, June 1949.

2791. Thornburn, D. B.: You can exercise after forty. *Hygeia, Chicago, 26:* 788-789; 824, 1948.
2792. Trimble, H.: Old lady refuses to be aged. *N. Y. Times Mag.*, Nov. 12, 1950, p. 14.
2793. Warren, M. W.: Activity in advancing years. *Brit. med. J., 2:* 921-924, 1950.
2794. Anonymous: Can business men lick old age? Interview with C. E. Dutchess. *Business Wk.*, Nov. 11, 1950, pp. 98-103.
2795. Anonymous: Emotional problems of the aged. *Amer. J. publ. Hlth., 40:* 1140-1142, 1950.
2796. Anonymous: Old people revitalized. *Sci. News Lett., Wash., 58:* 340, Nov. 25, 1950.

See also Nos. 2205, 3028, 3033, 3077.

VI. Premature Aging (Progeria)

2797. Force, B. R., and C. P. Powell: Progeria in the adult (Werner's syndrome); report of a a case. *U. S. Armed Forces med. J., 1:* 578-582, 1950.
2798. Manschot, W. A.: A case of progeronanism (progeria of Gilford). *Acta paediat., Stockh., 39:* 158-164, 1950.
2799. Oberdisse, K.: Senilität im Kindesalter. *Dtsch. Arch. klin. Med., 197:* 103-114, 1950.

PSYCHOLOGICAL PROCESSES

2800. Barnett, I.: The use of Z scores in equating the Wechsler-Bellevue sub-tests. *J. clin. Psychol., 6:* 184-188, 1950. Abstr: *P. A., 24:* No. 6347, 1950.
2801. Cover, C. B., and S. L. Pressey: Age and route sales efficiency. *J. appl. Psychol., 34:* 229-231, 1950.
2802. Fox, C., and J. E. Birren: The differential decline of subtest scores of the Wechsler-Bellevue intelligence scale in 60-69-year-old individuals. *J. genet. Psychol., 77:* 313-317, 1950.
2803. Gutman, B.: The application of the Wechsler-Bellevue scale in the diagnosis of organic brain disorders. *J. clin. Psychol., 6:* 195-198, 1950. Abstr: *P. A., 24:* No. 6479, 1950.
2804. Jalavisto, E.: Adaptation in the phantom limb phenomenon as influenced by the age of the amputees. *J. Geront., 5:* 339-342, 1950.
2805. Karsten, A.: (Psychology of aging.) *Geron. 1:* 15-23, 1949.
2806. Kass, W.: Wechsler's mental deterioration index in the diagnosis of organic brain disease. *Trans. Kansas Acad. Sci., 52:* 66-70, 1949. Abstr: *B. A., 24:* No. 18447, 1950.
2807. Lenz, L. L.: Über die Sexualität des alternden Mannes. *Zschr. Haut & Geschikr., 8:* 452-454, 1950.
2808. Mackworth, N. H.: *Researches on the measurement of human performance.* Med. Res. Counc., Spec. Rep. Ser. No. 268, Lond., 1950, 156 pp.
2809. Padalino, F.: Note di psicometria clinica; indice di sbilancio; coefficiente di deterioramento e metrica psi.. *Rass. Studi psichiat., 39:* 287-296, 1950.
2810. Pexiotto, H. E.: Wechsler-Bellevue sub-test patterns; a note of caution. *J. clin. Psychol., 6:* 188-190, 1950. Abstr: *P. A., 24:* No. 6359, 1950.
2811. Rappaport, S. R., and W. B. Webb: An attempt to study intellectual deterioration by premorbid and psychotic testing. *J. consult. Psychol., 14:* 95-98, 1950. Abstr: *P. A., 24:* No. 5975, 1950.
2812. Rogers, L. S.: A comparative evaluation of the Wechsler-Bellevue Mental Deterioration Index for various adult groups. *J. clin. Psychol., 6:* 199-202, 1950. *P. A., 24:* No. 6484, 1950.
2813. Rogers, L. S.: A note on Allen's index of deterioration. *J. clin. Psychol., 6:* 203, 1950. Abstr: *P. A., 24:* No. 6485, 1950.
2814. Shock, N. W.: The contribution of psychology. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 168-180.

See also Nos. 2734, 2758, 2778, 2793, 2795, 2856, 2930, 2936, 3011, 3020.

SOCIAL AND ECONOMIC ASPECTS

I. Accidents

2815. Collins, D. D.: Mortality in traumatic abdominal injuries in the elderly. *J. Geront., 5:* 241-244, 1950.
2816. Metrop. Life Insur. Co.: Accident toll high among females. *Statist. Bull. Metrop. Life Insur. Co., 31:* 7-9, Aug. 1950.
2817. National Safety Council: *Accident facts; 1950 edition.* The Council, Chicago, 1950, 96 pp.
2818. U. S. Federal Security Agency. Public Health Service. Office of Vital Statistics: Motor-vehicle accident fatalities; United States, 1948. *Vit. Statist., Spec. Rep., National Summaries, 35:* (15), 243-292, 1950.

III. Demography

2819. Bernert, E. H.: *Volume and composition of net migration from the rural-farm population, 1930-1940, for the United States; major geographic divisions and states.* U. S. Dept. Agric. Bur. Agric. Econ., Wash., Jan. 1944, 37 pp.
2820. Bogue, D. J.: Changes in population distribu-

tion since 1940. *Amer. J. Sociol., 56:* 43-57, July 1950.

2821. Capt, J. C.: Economic significance of population age shifts. *Comm. & Financ. Chron., 168:* 2080, 1948.

2822. Dublin, L. I.: The American population profile. *N. Y. Herald Tribune Forum,* Oct. 23, 1950, 10 pp. Also *in: Statist. Bull. Metrop. Life Insur. Co., 31:* 1-11, Oct. 1950.

2823. Edwards, W. H.: German age-problems. *Spectator, N. Y., & Chicago, 182:* 504-505, 1949.

2824. Hagood, M. J.: *Prospects for regional distribution of the population of the United States.* U. S. Dept. Agric., Bur. Agric. Econ., Wash., 1949, 8 pp.

2825. Pan, C.-L.: Demographic aspects of underdeveloped countries. *Ann. Amer. Acad. pol. soc. Sci., 270:* 42-50, July 1950.

2826. Shryock, H. S., Jr.: The changing age profile of the population. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 2-23.

2827. Smith, T. L.: The aged in rural society. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 40-53.

2828. Thompson, W. S.: Problems of population. *New Republic, 123:* 10-13, July 3, 1950.

2829. Tunkelo, A.: (Old people as a demographic factor.) *Geron, 1:* 5-14, 1949.

2830. U. S. Department of Agriculture: *Farm population estimates; January 1949.* Bur. Agric. Econ., Wash., June 1949, 8 pp.

2831. Whelpton, P. K.: A history of population growth in the United States. *Sci. Mon., N. Y., 27:* 277-288, Oct. 1948.

2832. Anonymous: Our aging population. *Spectator, N. Y., & Chicago, 156:* 44, Dec. 1948.

2833. Anonymous: Population front; 1950. *Biol. Human Affairs, 16:* 27-29, 1950.

2834. Anonymous: Problems confronting population commission. *U. N. Bull., 8:* 436, May 15, 1950.

See also No. 2189.

IV. Economic Problems

2835. Hildenbrand, G. C.: Geriatrics and the economic plight of our aging. *Amer. J. occup. Ther., 3:* 137-139, 1949.

2836. U. S. Federal Security Agency. Social Secuity Administration: *Resources of Old-Age and Survivors Insurance beneficiaries in Philadelphia and Baltimore; 1949.* Bur. of Old-Age & Surv. Insur., Div. Program Anal., Wash., May 1950, 33 pp.

IV-B. Economic Problems: *Employment*

2837. Amulree, V. W. S.: The employment of elderly workers. *Practitioner, 165:* 111-114, 1950.

2838. Barkin, S.: Union policies and the older worker. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 75-92.

2839. Brown, J. D.: The role of industry in relation to the older worker. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 65-74.

2840. California. State. Department of Employment: *Characteristics of unemployed and job openings; persons applying for nonfarm work through the California Department of employment compared with nonfarm job openings; week ending April 16, 1950.* The Department, Sacramento, 1950, 4 pp.

2841. Clague, E.: Some industrial aspects of aging. *Arch. industr. Hyg. & occup. Med., 2:* 189-195, 1950.

2842. Clague, E.: After 45, how about a job? *Survey, 86:* 173-176, April 1950.

2843. Desmond, T. C.: New idea for jobs at 65. *Rotarian, 76:* 27, May 1950. Also *in: Reader's Dig., 56:* 100-102, 1950.

2844. Gafafer, W. M.: Industrial sickness absenteeism.. *Publ. Hlth. Rep., Wash., 65:* 1556-1561, 1950.

2845. Geiger, A. J.: Coronary heart disease and the employee. *Industr. Med. & Surg., 19:* 509-511, 1950.

2846. Harris, B. R.: Rheumatic heart disease and employment. *Industr. Med. & Surg., 19:* 513-516, 1950.

2847. Kastner, R. P.: *Seniority rights for supervisors?* N. Y. (State) School of Industr. & Labor Relations, Res. Bull. No. 7, Ithaca, N. Y., 1950, 60 pp.

2848. Moore, W. E.: The aged in industrial societies. *In:* M. Derber, (Editor), *The Aged and Society, Industr. Rel. Ass.,* Champaign, Ill., 1950, pp. 24-39.

2849. Pharris, C.: Placement of the employee with cardiac and vascular disease in industry. *Industr. Med. & Surg., 19:* 523-527, 1950.

2850. Pollak, O. J.: The older worker in the labor market. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 56-64.

2851. Sayer, H. D.: Compensation act is no bar to elderly; rates do not reflect age of worker. *Eastern Underwriter, 49:* 81, Dec. 17, 1948.

2852. Speed, J. J., and J. J. Bambrick: *Seniority systems in nonunionized companies.* Nat Industr. Conf. Bd., N. Y., 1950, 32 pp.

2853. Stainbrook, E.: Psychological considerations in the rehabilitation of the cardiac patient in industry. *Industr. Med. & Surg., 19:* 528-531, 1950.
2854. U. S. Department of Agriculture: *Net movement away from farms in the United States, by age and sex; 1940-1944.* Bur. Agric. Econ. Series Census-BAE, No. 4, June 19, 1945, 1 p.
2855. U. S. Federal Security Agency. Social Security Administration: *Quarterly summary of wage employment and benefit data.* Bur. of Old-Age & Surv. Insur., Div. Prog. Anal., *10:* 1-20, Nov. 1950.
2856. Welford, A. T., and D. Speakman: The employability of older people. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 181-203.
2857. Wolfbein, S. L.: Measurement of work-life expectancy. *Mon. Labor Rev., 71:* 193-195, Aug. 1950.
2858. Wool, K.: Pattern of working life for men in 1940. *Mon. Labor Rev., 71:* 223-231, Sept. 1950.
2859. Anonymous: Back to work they go; retired scholars and professors. *Nat. educ. Ass., J., 39:* 548, 1950.
2860. Anonymous: Problems of the older workers; a symposium. *Employm. Sec. Rev., 17:* 3-16, Dec. 1950.
2861. Anonymous: Tables of working life. *U. S. Bur. Labor Bull.,* No. 1001, 1-74, 1950.

See also Nos. 2189, 2801.

IV-C. Economic Problems: *Retirement and Pensions*

(See also Social Security)

2862. Brannon, T. J., and E. K. Rowe: *Digest of selected health, insurance, welfare, and retirement plans under collective bargaining.* U. S. Bur. Labor Statist., Wash., July 1950, 52 pp.
2863. Canada. Bureau of Statistics. Health and Welfare Division: *Survey of pension and welfare plans in industry; 1947.* The Bu au, Ottawa, 1950, 101 pp.
2864. Cazac, G.: L'allocation-vieillesse du médecin; les commissions d'inaptitude. *Concours méd. 72:* 2149-2150, 1950.
2865. Ferrannini, L.: Invalidité et vieillesse. *Rev. méd. Liège, 5:* 717-718, 1950.
2866. Fitzgerald, T. A.: *Compensation and pensions for executives.* Nat. Indust. Conf. Bd., N. Y., 1950, 52 pp.
2867. Flannery, H. W.: California; pension paradise. *Commonweal, 50:* 110-113, May 1949.
2868. Haber, W.: After 65, what about an income? *Survey, 86:* 177-180, April 1950.
2869. Jodin, R.: Retraite et praticiens. *Concours méd., 72:* 2267-2268, 1950.
2870. Justin, J. J.: Pension plans; checklist for administrators. *Harv. Bus. Rev., 28:* 114-122, Nov. 1950.
2871. Kentucky. Legislative Research Commission: *A retirement system for Kentucky state employees.* Commonwealth of Kentucky, Frankfort, 1949.
2872. Lewis, F.: After retirement, what? *R. N., 13:* 26-27, Aug. 1950.
2873. Montgomery, D.: Pensions; in the American manner.. *J. Amer. Soc. Chartered Life Underwriters, 5:* 16-27, Dec. 1950.
2874. Moore, E. H.: Self provision for the aged. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 93-105.
2875. Randall, O. A.: Retirement, dead or alive? *Indep. Woman, 27:* 306-307, 1948.
2876. Slichter, S. H.: Retirement age and social policy. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 106-114.
2877. Stroock, M.: New model for pensions; General Motors' plan approaches the problem realistically. *Barron's, 30:* 7, Dec. 25, 1950.
2878. Terriberry, G. G.: *Establishing a pension plan.* Conf. on Labor, N. Y. Univ., 1950, pp. 121-143.
2879. Thompson, C. L.: What about old-age pensions? *Forum, 111:* 222-229, April 1949.
2880. Turner, P. A.: Yardstick for pension plans. *Eastern Underwriter, 49:* 8, Nov. 5, 1948.
2881. Wallace, W.: Trust plan; Sears, Roebuck & Co. *Factory Mgmt., 106:* 96-97, Nov. 1948.
2882. Witte, E. E.: Social provisions for the aged. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 115-136.
2883. Zorn, B. A.: *Bargaining over pensions.* Conf. on Labor, N. Y. Univ., 1950, pp. 103-119.
2884. Anonymous: Area pension plan perks up. *Business Wk.,* Nov. 4, 1950, p. 120.
2885. Anonymous: Area pensions in Detroit. *Business Wk.,* June 3, 1950, p. 86.
2886. Anonymous: Auto union yields on pensions. *U. S. News & World Rpt., 28:* 48, March 24, 1950.
2887. Anonymous: In Canada; $55. *Business Wk.,* April 29, 1950, p. 107.
2888. Anonymous: Canada. $40 for all, maybe. *Newsweek, 36:* 38, July 10, 1950.
2889. Anonymous: Chemical workers strike for U.N.W.-type pensions. *Business Wk.,* Aug. 19, 1950, p. 84.
2890. Anonymous: Collective bargaining provisions;

health, insurance, and pensions. *U. S. Bur. Labor Bull.*, No. 908, pt. 17, 102-222, 1950.

2891. Anonymous: Company pension and group-insurance plans; cost sharing. *Mon. Labor Rev., 70:* 298-299, March 1950.

2892. Anonymous: Ford, Nash pension deals. *Business Wk.*, March 25, 1950, pp. 113-114.

2893. Anonymous: G. M. paces the U. S. pension parade. *Life, 28:* 21-25, June 5, 1950.

2894. Anonymous: Miners gain. *U. S. News & World Rpt., 28:* 43, May 12, 1950.

2895. Anonymous: More workers qualify for National Steel's Retirement Program. *Iron Age, 162:* 145, 1948.

2896. Anonymous: New pension law for Canada. *Business Wk.*, Aug. 5, 1950, pp. 80-81.

2897. Anonymous: Ninety per cent of pension plans need to be revised. *Eastern Underwriter, 49:* 8, Nov. 26, 1948.

2898. Anonymous: Oil pension twist. *Business Wk.*, April 8, 1950, p. 103.

2899. Anonymous: Old hands snub pensions. *Business Wk.*, Nov. 18, 1950, pp. 124-125.

2900. Anonymous: Pension choice. *Business Wk.*, April 15, 1950, pp. 116-117.

2901. Anonymous: Pension plans spread, but statistics lag. *Business Wk.*, April 1, 1950, p. 88.

2902. Anonymous: Pension squeeze may ease. *Business Wk.*, May 6, 1950, p. 70.

2903. Anonymous: Pensions vs. pay raises as a lure for executives. *U. S. News & World Rpt., 28:* 18, June 2, 1950.

2904. Anonymous: Price of pensions. *Newsweek, 35:* 44, March 27, 1950.

2905. Anonymous: Private pension plans for railroad employees; 1949. *Mon. Labor Rev., 70:* 639-641, June 1950.

2906. Anonymous: Problem of payment and investment. *Newsweek, 35:* 72, March 27, 1950.

2907. Anonymous: Small-firm plan at Fesbert-Schorndorfer Co., Cleveland. *Business Wk.*, July 15, 1950, p. 91.

2908. Anonymous: Tax free pensions. *Business Wk.*, Dec. 2, 1950, p. 107.

2909. Anonymous: Twenty-five years of old age pensions; Young Women's Christian Association retirement fund. *Survey, 86:* 506, Nov. 1950.

2910. Anonymous: Unique pensions; Allegheny Ludlum makes top management men consultants at 65. *Business Wk.*, Dec. 4, 1948, p. 31.

See also Nos. 2180, 2940, 2944, 2968.

VI. Housing and Care

2912. Burstein, S. R.: Care of the aged in England, from medieval times to the end of the 16th century. *Bull. Hist. Med., 22:* 738-746, 1948.

2913. Gaman, J.: Home for the aged in Britain. *Soc. Serv. Rev., 22:* 101-102, 1948.

2914. Laverty, R.: Nonresident aid — community versus institutional care for older people. *J. Geront., 5:* 370-374, 1950.

2915. Mustala, P.: (The care of the old according to the present legislation.) *Geron, 1:* 24-32, 1949.

2916. National Conference of Catholic Charities: *Catholic institutional care of the aged.* The Conference, Wash., 1945, 43 pp.

2917. National Council of the Protestant Episcopal Church: *Episcopal church homes for the aged; a report based on study of information from forty-four church homes.* The Council, N. Y., 1947-1948.

2918. Swain, W. T., Jr.: The headquarters of a home for the aging. *Presbyterian home News, 14:* (2), 1-8, 1950.

2919. Anonymous: The cottage plan. *Presbyterian home News, 14:* (1), 1-8, 1949.

2920. Anonymous: Home and hospital; Motion Picture Relief Fund adds new medical facilities at Woodland Hills, California. *Archit. Forum, 89:* 104-108, 1948.

2921. Anonymous: Home for the Jewish aged, Kansas City, Missouri. *Archee Rec., 108:* 112-117, Dec. 1950.

2922. Anonymous: Ministers mecca; memorial home community. *Newsweek, 35:* 66, April 3, 1950.

See also Nos. 2189, 2260, 2780, 2933.

VIII. Medical Care

2923. Laidlaw, S.: The care and welfare of the aged and chronic sick. *J. R. sanit. Inst., 70:* 493-504, 1950.

2924. Lowe, C. R., and T. McKeown: The care of the chronic sick; social and demographic data. *Brit. J. soc. Med., 4:* 61-74, 1950.

2925. Mason, W. A.: Medical care and the "medically" needy. *J. nat. med. Ass., N. Y., 42:* 386-388, 1950.

2926. Sheldon, J. H.: Social medicine of old age. (Abstract). *Nature, Lond., 162:* 466, 1948.

2927. Sheldon, J. H.: Medical-social aspects of the aging process. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 219-237.

See also Nos. 2743, 2755, 2769.

IX. Social Problems
(includes social adjustment)

2928. Burgess, E. W.: Personal and social adjustment in old age. *In:* M. Derber, (Editor),

The Aged and Society, Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 138-156.

2929. Comerford, J.: *Health the unknown; the story of the Peckham experiment.* H. Hamilton, Lond., 1947, 144 pp.

2930. Cosin, L.: *Need for emotional adjustments in the elderly.* Nat. Counc. Soc. Serv., Inc., Lond., 1950, 20 pp.

2931. Harper, H. R.: *Toward a happier old age. Some highlights from the National conference on Aging held in Washington, D. C., August 13-15, 1950.* Denver, 1950, 19 pp.

2932. Havighurst, R. J.: Old folks take the spotlight. *Survey, 85:* 105-106, 1949.

2933. Herz, K. G.: *Eastern Pennsylvania study; the care of Jewish aged in the Allentown-Bethlehem-Easton-Reading area.* Counc. Jewish Fed. & Welf. Funds, Inc., N. Y., 1949.

2934. Portes, L.: Medicina e eutanásia. *J. méd., Pôrto, 16:* (392), 155-162, 1950.

2935. Roskam, J.: Survie purement végétative dans la cérébrosclérose. Euthanasie, dysthanasie, orthothanasie. *Rev. méd. Liège, 5:* 709-713, 1950.

2936. Samson, A. P., and W. G. Mather: *Personal and social adjustments of 49 retired rural men.* Penn. St. Coll. Agric. Exper. Sta., State College, Pa., 1950, 16 pp.

See also Nos. 2188, 2821.

X. Social Groups
(family, political, religious)

2937. Calder, R.: Revolt of the elders. *New Statesman & Nation, 36:* 234, Sept. 18, 1948.

2938. Fisher, L. H.: The politics of age. *In:* M. Derber, (Editor), *The Aged and Society,* Industr. Rel. Res. Ass., Champaign, Ill., 1950, pp. 157-167.

2939. Long, F., and C. Lucioli: Live long and like it club. *Wilson Libr. Bull., 23:* 301-305, 1948.

2940. Manning, R. E.: *The Townsend plan versus existing system of old-age security.* Lib. Congr., Legis. Ref. Serv., Wash., 1949, 24 pp.

2941. Maves, P. B.: *The Christian religious education of older people.* Fed. Counc. of Churches of Christ in Amer., N. Y., 1950, 96 pp.

2942. Maves, P. B.: The church in community planning for the aged. *Geriatrics, 5:* 339-342, 1950.

2943. Tuohy, E. L.: Gerontocracy. *Geriatrics, 5:* 337-338, 1950.

2944. Washington. State. Department of Social Security. *Citizen's Security Act of 1948.* Initiative Measure No. 172, 1949.

2945. Anonymous: *Churches' part in old peoples' welfare.* Bull. Central Churches Group, Lond., April 1947, 8 pp.

2946. Anonymous: Elder-ages; recreation in Philadelphia. *Ladies Home J., 65:* 23, Nov. 1948.

2947. Anonymous: Ham-and-eggs hangover in Oregon. *Newsweek, 33:* 23, Feb. 21, 1949.

2948. Anonymous: Initiative goes haywire. *Fortune, 39:* 83-85, March 1949.

2949. Anonymous: Townsend and friends. *Newsweek, 31:* 27, June 14, 1948.

2950. Anonymous: Turbulent middle years, subject of Vassar's seminar in family living. *Survey, 86:* 204-205, April 1950.

See also Nos. 2784, 2827.

XI. Social Security

2951. Aiello, G.: Problèmes médico-sociaux en termes d' invalidité et vieillesse. *Rev. méd. Liège, 5:* 713-715, 1950.

2952. Burns, E. M.: Our new social security. *Survey, 86:* 429-433, 1950.

2953. Cerny, F.: Social insurance in Rumania. *Bull. Int. Soc. Sec. Ass., Year III,* Nos. 8-9, 1-10, Aug.-Sept. 1950.

2954. Chatters, C. H.: Extension of Social Security benefits urged for municipal employees. *Amer. City, 65:* 9, March 1950.

2955. Cohen, W. J.: The Social Security Act Amendments of 1950. *Publ. Welfare, 8:* 226-230, 1950.

2956. Cohen, W. J.: Security for old age; aspects of legislative history of the Social Security Act Amendments of 1950. *Industr. & Labor Relations Rev., 4:* 187-199, Jan. 1951.

2957. Corson, J. J.: Social Security needs modernizing. *New Republic, 122:* 10-12, May 8, 1950.

2958. Eberling, E. J.: Old-Age and Survivor's Insurance and old age assistance in the South. *Sth. econ. J., 15:* 54-66, July 1948.

2959. Fauri, F. F.: *Old-age and Survivors Insurance; coverage, eligibility requirements, and benefit payments.* U. S. Congress, Senate, Comm. on Finance, U. S. Govt. Print. Off., Wash., 1950, 20 pp.

2960. Folsom, M. B.: Money after age 65. *Atlantic Mon., 184:* 69-72, Aug. 1949.

2961. Greenough, W. C.: Social security for educators. *Bull. Amer. Ass. Univ. Professors, 36:* (3), 558-576, 1950.

2962. Hohaus, R. A.: Recent Social Security amendments; an appraisal. *Amer. econ. Sec., 7:* 10-20, Nov.-Dec. 1950.

2963. International Social Security Agreements: Agreements signed by France with Yugoslavia, the Netherlands, and the United Kingdom (Northern Ireland). *Industr. Labour, 4:* 300-301, 1950.

2964. Keyes, J. M.: What about draftees' pensions? Reply with rejoinder. *Business Wk.*, Nov. 4, 1950, p. 92.

2965. Lasser, J. K.: For broader and deeper social security. *N. Y. Times Mag.*, Nov. 14, 1948, p. 26.

2966. Marrot, J.: Organisation de la sécurité sociale dans le monde. *Médecin fr., 10:* 191-194, 1950.

2967. National Education Association of the United States. Research Division: *Some immediate problems with respect to teacher retirement and social security.* The Association, Wash., 1950, 7 pp.

2968. Ontario. Department of Public Welfare: *Public welfare in Ontario, old-age pensions, blind pensions, public assistance, soldiers' aid, homes for aged, children's institutions, mothers' allowances, children's aid, and day nurseries.* The Department, Ontario, 1950, 20 pp.

2969. Perlman, J.: Federal program of Old-Age and Survivors Insurance. *Mon. Labor Bull., 982:* 1-8, 1950.

2970. Perlman, J.: Security for old age; changing trends under Old-Age and Survivors Insurance, 1935-1950. *Industr. & Labor Relations Rev., 4:* 173-186, Jan. 1951.

2971. Permanent Inter-American Committee on Social Security: *The Inter-American committee on social security; origin, creation, constituent agencies, publications, financial resources, international relations, resolutions and their effects.* International Labour Office, Geneva, 1950, 94 pp.

2972. Reed, G. E.: Old Age and Survivors Insurance. *Hosp. Prog., 31:* 222-223, 1950.

2973. Research Council for Economic Security: *Views and ideas; review of recent comments and ideas in the field of economic security.* The Council, Chicago, 1950, 15 pp.

2974. Ulman, R.: *Federal security planning.* Univ. Debaters Annual, 1947-1948, pp. 285-322.

2975. United Nations. Economic and Social Council: *Welfare of the aged; old age rights. Summarized documentation on measures for the benefit of aged persons and the effect of such measures on their standard of living. Report by the secretary-general to the social commission and the commission on human rights.* The Council, Jan. 1950, 104 pp.

2976. U. S. Bureau of Internal Revenue: *Household employer's Social Security tax guide. Instructions for the reporting and payment of employer and employee taxes on the wages of household employees.* U. S. Govt. Print. Off., Wash., 1950, 15 pp.

2977. U. S. Bureau of Old-Age and Survivors Insurance: *Background material; Old-Age and Survivors Insurance.* The Bureau, Wash., 1950, 12 pp.

2978. U. S. Social Security Administration: *Social Security Yearbook, 1948. Annual supplement to the Social Security Bulletin.* U. S. Govt. Print. Off., Wash., 1950, 60 pp.

2979. U. S. Social Security Administration: *Some basic readings in social security;* 1950 Supplement. U. S. Govt. Print. Off., Wash., 1950, 55 pp.

2980. Whecler, W. H.: Let's merchandise security; with discussion. *Rotarian, 77:* 12-15, July 2, 1950.

2981. Anonymous: Agreement supplementary to the Franco-British Social Security agreement. *Industr. Labour, 3:* 467-468, 1950.

2982. Anonymous: All about the big new pensions. *U. S. News & World Rpt., 28:* 14-15, June 30, 1950.

2983. Anonymous: Bigger pensions by November 1. *U. S. News & World Rpt., 29:* 24-25, July 28, 1950.

2984. Anonymous: Bigger pensions; some tax gaining favor in Senate. *U. S. News & World Rpt., 28:* 52-55, April 14, 1950.

2985. Anonymous: Billions in pension demands. *U. S. News & World Rpt., 25:* 28, Nov. 5, 1948.

2986. Anonymous: Ceilings increased on aid for the aged and blind. *Publ. Aid Ill., 16:* 1, 1949.

2987. Anonymous: More security for many. *Newsweek, 36:* 32, Sept. 11, 1950.

2988. Anonymous: New Social Security law; its effect upon teacher retirement. *Nat. educ. Ass. J., 39:* 506, 1950.

2989. Anonymous: Old age pensions; how big; who should pay for them. *Time, 55:* 26-27, May 22, 1950.

2990. Anonymous: One-fourth of workers under pension plans; analysis by Treasury Department. *Eastern Underwriter, 49:* 10, Nov. 1948.

2991. Anonymous: Public social security programs in the U. S.; 1949-1950. *Mon. Labor Rev., 70:* 1-13; 132-139; 257-262, Jan.-Mar. 1950.

2992. Anonymous: Reform of compulsory social insurance in Peru. *Industr. Labour, 4:* 306-307, 1950.

2993. Anonymous: Reorganization of the social security scheme in Poland. *Industr. Labour, 4:* 426-427, 1950.

2994. Anonymous: *Social Security Act Amendments of 1950. Public law 734, 81st Congress, Second Session.* U. S. Govt. Print. Off., Wash., 1950, 94 pp.

2995. Anonymous: Social security in Czechoslovakia. *Int. Labour Rev., 58:* 151-186, 1948.

2996. Anonymous: Social security in Czechoslovakia

—the history of national insurance up-to-date. *Nat. Insur. Gaz., 37:* 464-465, 1948.

2997. Anonymous: Social security in France and in the overseas "Departments". *Industr. Labour, 4:* 454-457, 1950.

2998. Anonymous: Social Security reaches the municipality. *Amer. City, 65:* 123, Nov. 1950.

2999. Anonymous: Social Security rides a boom. New changes and how they will be applied. *Scholastic, 57:* 10-11, Dec. 13, 1950.

3000. Anonymous: We've been asked about broader old-age pay. *U. S. News & World Rpt., 28:* 46, May 5, 1950.

3001. Anonymous: We've been asked about maids' Social Security. *U. S. News & World Rpt., 29:* 50-51, Dec. 8, 1950.

3002. Anonymous: We've been asked what Social Security changes mean. *U. S. News & World Rpt., 29:* 45, Sept. 1, 1950.

3003. Anonymous: We've been asked who now gets old-age aid. *U. S. News & World Rpt., 29:* 54-55, Aug. 4, 1950.

3004. Anonymous: What about draftees' pensions. *Business Wk.,* Oct. 7, 1950, p. 124.

3005. Anonymous: Your share in the new Social Security; legislation that will interest every nurse in the United States. *Nurs. World, 124:* 357, 1950.

XII. Social Services and Social Work (recreation and rehabilitation)

3006. Addis, R. S.: Training and scope of the psychiatric social worker in relation to adults. *Ment. Hlth., Lond., 8:* 63-66, 1949. Abstr: *P. A., 24:* No. 5849, 1950.

3007. Boucher, A. B., and J. L. Tehan: No one under sixty need apply; Hodson Community Center, Bronx, New York. *Recreation, 42:* 347-350, 1948.

3008. Bowen, G. E.: *A place in the sun.* Phil. Recreation Ass., Phil., 1950, 28 pp.

3009. Bowen, G. E.: *An ideal job for the volunteer.* Phil. Recreation Ass., Phil., 1950, 5 pp.

3010. Bowen, G. E.: Time of their lives; recreation for Philadelphia's older people. *Recreation, 44:* 375-378, Dec. 1950.

3011. Burstein, S. R.: Lillien Jane Martin (1851-1943); pioneer in old age rehabilitation. *Med. Illustr., 4:* (2), 82-90, 1950.

3012. Committee on the Aging: *Community action for the aging.* N. Y. St. Ass. of Counc. of Soc. Agencies, N. Y., 1950, 15 pp.

3013. Cosin, L. A.: Geriatric rehabilitation. *Geriatrics, 3:* 294-295, 1948. Also *in: Brit. J. phys. Med., 2:* 162-167, 1948.

3014. Douglass, J. H., and R. H. Roberts: *Projects in woodwork.* McKnight & McKnight, Bloomington, Ill., 1948, 135 pp.

3015. Ferderber, M. B.: Medical rehabilitation of the physically handicapped. *Penn. med. J., 53:* 473-477, 1950.

3016. Grayson, M.: The concept of "acceptance" in physical rehabilitation. *Milit. Surg., 107:* 221-226, 1950.

3017. Kursen, F. H.: The scope and future of physical medicine and rehabilitation. *J. Amer. med. Ass., 144:* 727-732, 1950.

3018. Morris, E. L.: "Rehabilitation team" needs new members. *Occupational Trends, 2:* 2-10, Sept.-Oct. 1950.

3019. Puerto Rico. Department of Health. Division of Public Welfare: *Por los ninos, los ancianos, los impedidos, 1949-1950.* The Department, San Juan, 1950, 18 pp.

3020. Reedy, C.: Vocational rehabilitation. *Amer. J. publ. Hlth., 40:* 966-968, 1950.

3021. Rusk, H. A.: What can you do for the chronic? *G. P., 2:* (2), 43-49, 1950.

3022. Rusk, H. A.: Physical medicine and rehabilitation in medical education. *J. Amer. med Ass., 144:* 730-732, 1950.

3023. Sensenich, H.: Team work in rehabilitation. *Amer. J. publ. Hlth., 40:* 969-972, 1950.

3024. Stevens, A. L.: Work evaluation in rehabilitation. *Occup. Ther., 29:* 157-161, 1950.

3026. Anonymous: Community Center Services for the elderly; report of survey. *Recreation, 44:* 57, May 1950.

3027. Anonymous: Ideas for activities with the elderly. *Recreation, 44:* 80-82, May 1950.

3028. Anonymous: They live on their interests; conclusion of four-year study of elderly people. *Hobbies, 55:* 55, Dec. 1950.

See also Nos. 2451, 2461, 2462, 2753, 2782, 2853, 2942, 2946.

MISCELLANEOUS

3029. Bonis, A., and J. Moroy: Le vieillissement artificiel des eaux de vie. *Ann. Falsificat. et Fraudes, 41:* 380-383, 1948. Abstr: *B. A., 24:* No. 22995, 1950.

3030. Brockmann, M. C.: Relationship between acids, esters, and solids during the aging of whisky. *J. Ass. offic. agric. Chem., 33:* 127-129, 1950. Abstr: *B. A., 24:* No. 22996, 1950.

3031. Ferrannini, L.: Activité du centre de médicine de la vieillesse de Bari. *Rev. Méd. Liège, 5:* 731-732, 1950.

3032. Marvin, H. M.: *You and your heart; a clinic for laymen on the heart and circulation.* Random House, N. Y., 1950, 306 pp.

3033. Nesbit, R. M.: *"Your prostate gland"; letters from a surgeon to his father.* C. C. Thomas, Springfield, 1st ed., 1950, ix, 50 pp.

3034. Thurstone, J. L.: Security for old age: First national conference on aging; a preview of maturity. *Industr. & Labor Relations Rev., 4:* 163-172, Jan. 1951.

3035. Anonymous: Le vieillissement des sérums. *Sem. Hôp. Paris, 26:* 2349-2350, 1950.

See also Nos. 2178, 2184, 2191, 2931.

IV. Popular Articles

3036. Adams, S. H.: Old age; I spit in his eye. *Saturday Evening Post, 222:* 31, May 27, 1950.

3037. Ashton, E. H.: National myth; that everyone can provide his own security. *Survey, 84:* 359, Dec. 1948.

3038. Backus, E. B.: Grow old along with me. *Publ. Welf. Indiana, 60:* (11), 5-7; 14-15, 1950.

3039. Beck, B. Z.: Young at forty-five. *Today's Hlth., 28:* 44-45, May 1950.

3041. Bryant, A.: How best to grow old. *Illustr. London News, 213:* 450, Oct. 1948.

3042. Cave, M.: Stray notes at seventy. *Good Housekeeping, 129:* 113, Oct. 1949.

3043. Clancy, L. B.: Happiest time of life. *Today's Hlth., 28:* 34-35, July 1950.

3044. Cole, S.: Facing forty. *Good Housekeeping, 128:* 38, June 1949.

3045. Davidson, C.: Act your age. *Vital Speeches of the Day, 14:* 731-734, 1948.

3046. Davis, W.: From now on; oldsters. *Sci. News Lett., Wash., 57:* 354, June 10, 1950.

3047. Dock, G., Jr.: Mirage of pensions; reply. *Harper's Mon. Mag., 200:* 24, April 1950.

3048. Dublin, L. I., and H. Yahraes: When you're old — what then? II. Adding life to the added years. III. Life can begin at 65. *Colliers, 127:* (1), 16-17; 39-40, Jan. 6, 1951. *Ibid:* (2), 24-25; 72-73, Jan. 13, 1951, and (3), 26-27; 65-66, Jan. 20, 1951.

3049. Evans, W.: You may live to be 147. *True Story, 63:* 46-47; 90; 92-93, Dec. 1950.

3050. Flynn, C. E.: Notes on reaching forty; with comment by W. B. Pitkin. *Rotarian, 73:* 25-26, Oct. 1948.

3051. Galton, L.: Should you have children after 35? *Better Homes and Gardens, 26:* 42-43, July 1948.

3052. Goldberg, R.: On the privilege of being over sixty. *Rotarian, 77:* 12-14, Oct. 1950.

3053. Gumpert, M.: Future of old age. *Sci. Illustr., 1:* 37-40, 1946.

3054. Gumpert, M.: Mental disturbance and old age. *Nation, 167:* 695-696, 1948.

3055. Gumpert, M.: Our unknown aged. *Nation, 171:* 182-183, Aug. 26, 1950.

3056. Gumpert, M.: Recharting life for an aging America. *N. Y. Times Mag.,* Aug. 13, 1950, p. 12.

3057. Gumpert, M., and D. Lang: Profiles; geriatrician. *New Yorker, 26:* 30-34, June 10, 1950. *Ibid:* 34-36, June 17, 1950.

3058. Hill, M. N.: Care of the aged. *Spectator, N. Y., & Chicago, 181:* 400, 1948.

3059. Jacobson, M.: Old age is your problem. *Reader's Dig., 57:* 46-50, Nov. 1950.

3060. Lawton, G.: After 30. *Amer. Mag., 146:* 148, Oct. 1948.

3061. Lawton, G.: What do you mean old? *Amer. Home, 44:* 23, June 1950.

3062. Michener, J. A.: Out of pasture. *Nations' Bus., 37:* 32-33, April 1949.

3063. Miller, R. I.: Exercise after 40? Yes. *Sci. Digest, 28:* 45-47, Nov. 1950.

3064. Popkin, Z.: Widows and the perilous years. *Harper's Mon. Mag., 199:* (1129), 69-75, 1949.

3065. Rawlings, C.: Old sailors never die. *Nation's Bus., 37:* 40-42, May 1949.

3066. Robinson, M.: Magna charta for aging. *Survey, 86:* 448-452, Oct. 1950.

3067. Rorty, J.: Thin rats bury the fat rats. *Harper's Mon. Mag., 198:* 28-34, May 1949.

3068. Smith, H.: Youth must be served; American obsessed by dream of perpetual youth. *Saturday Rev. Literat., 31:* 20, Oct. 2, 1948.

3069. Smith, W. M., Jr.: So old nobody wants you. *J. home Econ., 41:* 308-310, 1949.

3070. Strattan, E.: Is old age necessary? *Today's Hlth., 28:* 32-33, Nov. 1950.

3071. Anonymous: After 40 life's no longer. *U. S. News & World Rpt., 28:* 22-23, March 24, 1950.

3072. Anonymous: Battle for pensions. *Life, 27:* 41-45, Oct. 17, 1949.

3073. Anonymous: Beware of age categories. *Life, 28:* 34, June 19, 1950.

3074. Anonymous: Bigger and better pensions? *U. S. News & World Rpt., 27:* 29-30, Sept. 30, 1949.

3075. Anonymous: Happier life after 60. *Sci. Digest, 27:* 9-13, June 1950.

3076. Anonymous: How much longer will you live? *Reader's Dig., 57:* 92, Aug. 1950.

3077. Anonymous: Is there a key to long life? *Sci. Digest, 25:* 74-75, June 1949.

3078. Anonymous: Magic dime. *Fortune, 41:* 20, March 1950.

3079. Anonymous: Making aged healthy seen as way to lasting peace. *Sci. News Lett., Wash., 55:* 205, 1949.

3080. Anonymous: Not so withered with age; studies

of nonagenarians and centenarians. *Newsweek, 34:* 42-43, July 11, 1949.

3081. Anonymous: Nothing's too good for grandpa *Time, 54:* 16-17, Sept. 5, 1949.

3082. Anonymous: Old man, tired and sick, guide postwar world in atomic age. *U. S. News & World Rpt., 27:* 34-35, Sept. 23, 1949.

3083. Anonymous: Older and better. *Newsweek, 32:* 72, Sept. 20, 1948.

3084. Anonymous: Quirks in giving age. *Sci Digest, 24:* 39, Nov. 1948.

3085. Anonymous: Ready to retire? *Business Wk.,* April 30, 1949, p. 124.

3086. Anonymous: Ripe old age. *Sci. Illustr., 3:* 112, 1948.

3087. Anonymous: Rising demand for pension plans. *U. S. News & World Rpt., 24:* 45-46, April 23, 1948.

3088. Anonymous: Senile statistics. *Time, 52:* 72, Nov. 29, 1948.

3089. Anonymous: Speaking of pictures; veterans left from the Civil War. *Life, 26:* 8-9, May 30, 1949.

3090. Anonymous: Surgery OK for oldsters. *Sci. Digest, 29:* 51, Jan. 1951.

3091. Anonymous: Three decades to add years to our lives. *Sci. News Lett., Wash., 54:* 402, 1948.

3092. Anonymous: West may need Chinese attitude toward old age. *Sci. News Lett., Wash., 25:* 38, April 1949.

3093. Anonymous: Why not recruit retired experts for state jobs. *Saturday Evening Post, 222:* 10, April 1, 1950.

See also Nos. 2201, 2210, 2215, 2220, 2786, 2792, 2794, 2842.